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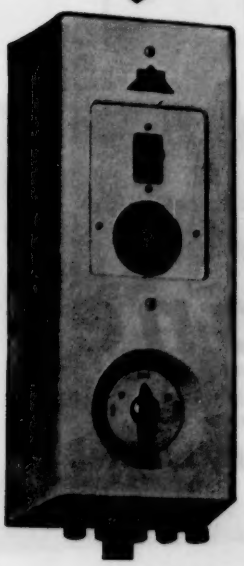

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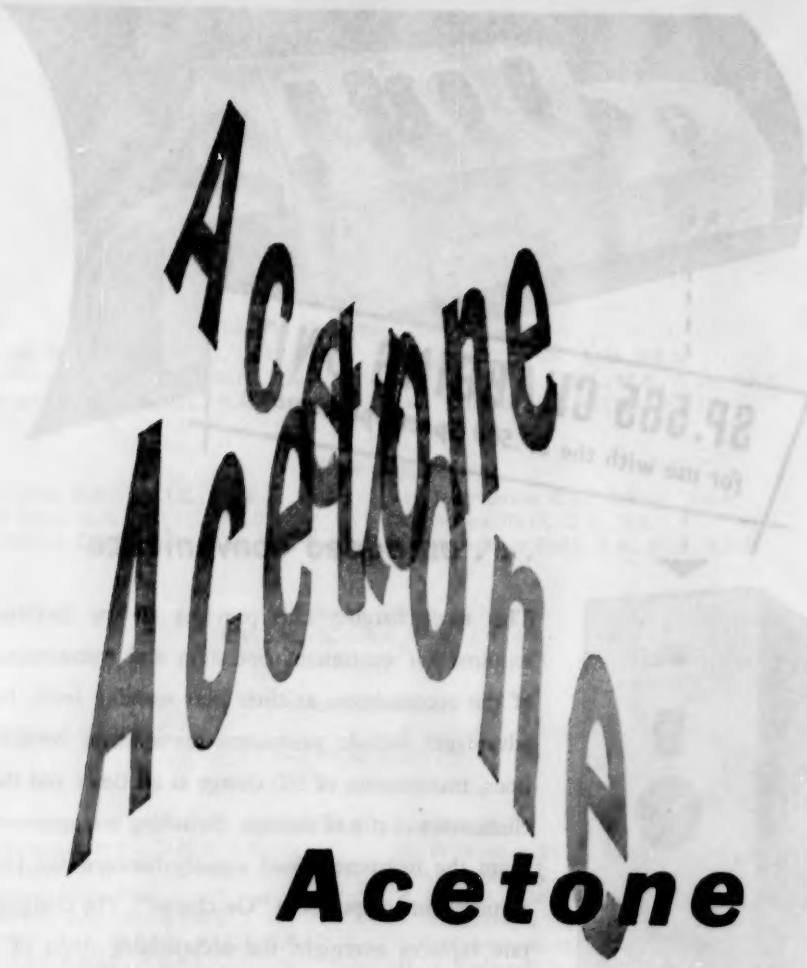


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**PHYSICAL PROPERTIES**

| | |
|---|---|
| Boiling Point (760 mm.) | 19.9°C |
| Freezing Point | −83°C |
| Specific Gravity (Liquid 0°C) | 1.01 |
| Specific Heat (Liquid 0°C) | 0.85 |

The vapour is polymerised to a degree which varies rapidly with temperature and pressure producing a corresponding variation in the heat of vaporisation.

**SPECIFICATION**

The normal grade of AHF contains at least 99% HF, and impurities to the following limits:—

| | |
|---|---|
| $H_2O$ | 0.5% max. |
| $SO_2$ | 0.25% max. |
| Si (calc. as $SiF_4$) | 0.25% max. |
| $H_2SO_4$ | 0.01% max. |
| $H_2S$ | may be present in traces. |

Higher grades up to 99.9% HF can be supplied according to need.

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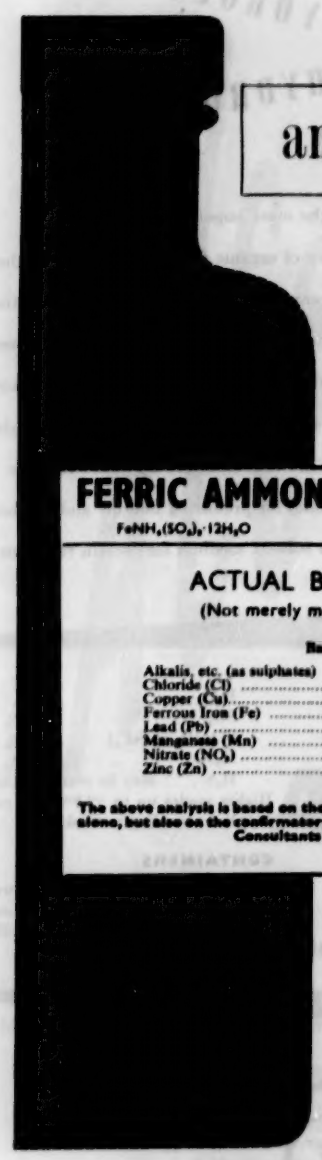

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$FeNH_4(SO_4)_2 \cdot 12H_2O$ Mol. Wt. 482·21

ACTUAL BATCH ANALYSIS

(Not merely maximum impurity values)

Batch No. 41603

| | |
|---|---|
| Alkalis, etc. (as sulphates) | 0·031% |
| Chloride (Cl) | 0·0001% |
| Copper (Cu) | 0·0003% |
| Ferrous Iron (Fe) | no reaction |
| Lead (Pb) | no reaction |
| Manganese (Mn) | 0·004% |
| Nitrate ($NO_3$) | 0·0005% |
| Zinc (Zn) | 0·003% |

The above analysis is based on the results, not of our own Control Laboratories alone, but also on the confirmatory Analytical Certificate issued by independent Consultants of international repute

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## 718. *Synthesis of Lapachenole.*

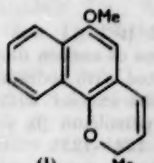
By R. Livingstone and R. B. Watson.

The synthesis by two independent routes is described of 4′-methoxy-6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran (I) which is identical with lapachenole [1] isolated from the heartwood of " Brazilian white peroba " (*Paratecoma alba*).

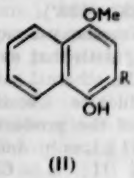
The first method for the synthesis of 4′-methoxy-6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran (I) was based on the formation of the coumarin system from 1-hydroxy-4-methoxy-2-naphthaldehyde (II; R = CHO). Friedlander's method [2] for the preparation of the aldehyde (II; R = CHO) could not be repeated and the sodium–amalgam reduction of 1-hydroxy-4-methoxy-2-naphthoic acid (II; R = $CO_2H$) was therefore considered. Weil [3] obtained a 60% yield of salicylaldehyde from salicylic acid in the presence of boric acid and a primary amine; this method also gave good yields with 1-hydroxy-2-naphthoic acid and 2 : 3-, 2 : 5-, and 2 : 4-hydroxytoluic acids but failed with 1-naphthoic acid, 3-acetoxy-2-naphthoic acid, and quinol- and pyrogallol-carboxylic acids.

The acid (II; R = $CO_2H$) was eventually prepared by Homeyer and Wallingford's method [4] from 1 : 4-dihydroxy-2-naphthoic acid. Reduction of the acid (II; R = $CO_2H$) by 2½% sodium amalgam gave only a 3% yield of the aldehyde (II; R = CHO). Preparation from 4-methoxy-1-naphthol by Reimer–Tiemann reaction as developed by Rubenstein,[5] and from methyl 1-hydroxy-4-methoxy-2-naphthoate (IIIc) by the McFadyen–Stevens method [6] both gave a 2% yield of the desired aldehyde.

Methyl 1-hydroxy-4-methoxy-2-naphthoate was therefore reduced to 2-hydroxymethyl-4-methoxy-1-naphthol (II; R = $CH_2$·OH) by means of lithium aluminium hydride, in 45% yield when Nystrom and Brown's [7] method was followed. Direct reduction of the acid (II; R = $CO_2H$) with lithium aluminium hydride gave alcohol (II; R = $CH_2$·OH) in 35% yield.



(I)



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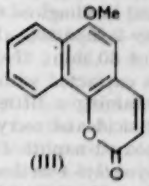


(III)

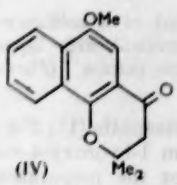
This was then oxidised by the Oppenauer method, *p*-benzoquinone being used as hydrogen acceptor, in 52% yield, and the aldehyde (II; R = CHO) was then converted into 6-methoxy-7 : 8-benzocoumarin (III) by Perkin's method. Attempts to prepare the benzocoumarin (III) from 4-methoxy-1-naphthol, malic acid, and concentrated sulphuric acid failed to give any identifiable product. 4-Methoxy-1-naphthol was prepared in 88% yield by the decarboxylation of 1-hydroxy-4-methoxy-2-naphthoic acid.

Reaction of 6-methoxy-7 : 8-benzocoumarin (III) with excess of methylmagnesium iodide gave 4′-methoxy-6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran as a gum; decomposition of its picrate by chromatography gave a product identical with lapachenole (I). The identity of the product was also confirmed by treatment with formic acid, giving lapachenole dimer.[1]

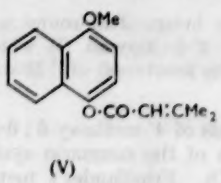
In the second synthesis, 6-methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-one (IV) was obtained by an extension of the method for the preparation of substituted chromanones.[8]

[1] Livingstone and Whiting, *J.*, 1955, 3631.
[2] Friedlander, *Ber.*, 1908, **41**, 1035.
[3] Weil, *ibid.*, p. 4147; 1921, **54**, 3217; 1922, **55**, 224, 2664.
[4] Homeyer and Wallingford, *J. Amer. Chem. Soc.*, 1942, **64**, 798.
[5] Rubenstein, *J.*, 1925, **127**, 1998.
[6] McFadyen and Stevens, *J.*, 1936, 584.
[7] Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 2548.
[8] Cavill, Dean, McGookin, Marshall, and Robertson, *J.*, 1954, 4573.

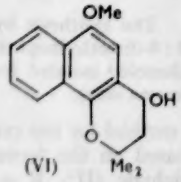
Esterification of 4-methoxy-1-naphthol with ββ-dimethylacryloyl chloride [9,10] by Fries rearrangement of the product (V) in the absence of solvent, followed by acidic isomerisation and ring closure, gave the benzochromanone (IV). Reduction by lithium aluminium



(IV)



(V)



(VI)

hydride readily gave the corresponding chromanol (VI). The removal of water by Klages's method [10] or with acetic anhydride was unsuccessful but on treatment with syrupy phosphoric acid lapachenole dimer was obtained.

Pyrolysis of the acetate of (VI) gave lapachenole.

## Experimental

*1-Hydroxy-4-methoxy-2-naphthoic Acid* (II; R = $CO_2H$) *and Methyl 1-Hydroxy-4-methoxy-2-naphthoate.*—1 : 4-Dihydroxy-2-naphthoic acid [4] (20 g.) in methanol (280 g.) was cooled in ice and saturated with dry hydrogen chloride. The solution was refluxed for 3 hr., cooled, and resaturated with hydrogen chloride. After 18 hr. at room temperature, the mixture was added to water and the solid filtered off, washed, and dried.

An ethereal solution of the product was extracted with dilute sodium hydrogen carbonate solution; acidification of the extract and recrystallisation from aqueous ethanol gave 1-hydroxy-4-methoxy-2-naphthoic acid (6·1 g.), m. p. 194—196° (decomp.) [Homeyer and Wallingford [4] give m. p. 196—198° (decomp.)].

Evaporation of solvent from the ethereal fraction gave methyl 1-hydroxy-4-methoxy-2-naphthoate (10·9 g.), forming pale cream needles, m. p. 136—138° after recrystallisation (Homeyer and Wallingford [4] give m. p. 137—138°).

*4-Methoxy-1-naphthol.*—1-Hydroxy-4-methoxy-2-naphthoic acid (6·2 g.) was heated at 210—215° for 30 min., the loss agreeing with that expected for loss of carbon dioxide. The product was extracted with ether and the ethereal solution extracted with sodium hydroxide solution containing a little sodium dithionite. Acidification of the extract with ice-dilute hydrochloric acid and recrystallisation of the product from light petroleum (b. p. 80—100°) gave 4-methoxy-1-naphthol as needles (4·1 g.), m. p. and mixed m. p. 124—125°.

*2-Hydroxymethyl-4-methoxy-1-naphthol* (II; R = $CH_2$·OH).—(1) A suspension of lithium aluminium hydride (0·9 g.) in dry ether (230 c.c.) was boiled in a flask equipped with a Soxhlet extractor containing methyl 1-hydroxy-4-methoxy-2-naphthoate (4 g.) in the thimble. After 2½ hr. the mixture was cooled and water added, followed by ice–10% sulphuric acid. The ethereal layer was washed with water and dried. Removal of solvent and recrystallisation of the residue from chloroform–light petroleum (b. p. 80—100°) gave needles (1·6 g.), m. p. 95—97° of the *alcohol* (Found: C, 71·3; H, 5·85. $C_{13}H_{12}O_3$ requires C, 70·6; H, 5·9%).

(2) 1-Hydroxy-4-methoxy-2-naphthoic acid (4·3 g.) was reduced in the same way. After the decomposition of the complex, the ethereal layer was separated and extracted with sodium hydrogen carbonate solution. This aqueous solution when acidified gave 1-hydroxy-4-methoxy-2-naphthoic acid (1·35 g.). The ethereal solution was washed with water and dried. Evaporation of solvent and crystallisation of the product from chloroform–light petroleum (b. p. 80—100°) gave 2-hydroxymethyl-4-methoxy-1-naphthol (1·4 g.), m. p. 95—97°.

*1-Hydroxy-4-methoxy-2-naphthaldehyde* (II; R = CHO).—A solution of aluminium *tert.*-butoxide (1·2 g.) in dry benzene (30 c.c.) was added to one of 2-hydroxymethyl-4-methoxy-1-naphthol (2·7 g.) and *p*-benzoquinone (4 g.) in dry benzene (30 c.c.). The solution was refluxed for 1 hr. and the excess of benzene and *p*-benzoquinone then removed by steam distillation. The flask was cooled, concentrated sulphuric acid (2 c.c.) added, and the reaction mixture then steam-distilled for a further 6—8 hr. The yellow solid in the distillate was recrystallised from

[9] Bridge, Heys, and Robertson, *J.*, 1937, 283.
[10] Klages, *Ber.*, 1904, **37**, 3987.

petroleum (b. p. 60—80°), giving 1-hydroxy-4-methoxy-2-naphthaldehyde (5·2 g., 52%) as yellow needles, m. p. 99—100° (Friedlander [3] gives m. p. 100°).

*6-Methoxy-7 : 8-benzocoumarin* (III). 1-Hydroxy-4-methoxy-2-naphthaldehyde (6 g.), acetic anhydride (6·5 c.c.), fused potassium acetate (3 g.), and iodine (0·05 g.) were heated at 120—125° for 2 hr., and then at 165—170° for 5 hr. The mixture was poured into warm water and set aside overnight. The solid was filtered off, washed with 2% sodium hydroxide solution (50 c.c.) and then water, dried, and crystallised from acetic acid by addition of water. *6-Methoxy-7 : 8-benzocoumarin* (3·8 g., 56%) formed fine yellowish-white needles, m. p. 132—134° (Found : C, 74·4; H, 4·7. $C_{14}H_{10}O_3$ requires C, 74·3; H, 4·4%); its solution in concentrated sulphuric acid was yellowish-green with a slight greenish-blue fluorescence.

*4′-Methoxy-6 : 6-dimethylnaphtho(1′ : 2′-2 : 3)pyran.*—6-Methoxy-7 : 8-benzocoumarin (3·7 g.) in dry benzene (100 c.c.) was added slowly (1 hour) to a stirred Grignard solution prepared from methyl iodide (9·7 g.), magnesium (1·8 g.), and ether (80 c.c.). The reddish solution was refluxed for 1 hr. and then set aside overnight. Decomposition by 22% ammonium chloride solution (75 c.c.) and extraction with ether gave a red ethereal solution, which was washed with water and dried ($CaCl_2$). Removal of solvent and distillation of the residue gave an oil (0·7 g.), b. p. 130—150°/20 mm.

Steam-distillation of the product (0·48 g.) gave a volatile fraction (0·23 g.), which again did not solidify. Addition of a saturated methanolic solution of picric acid and crystallisation from methanol gave dark-violet needles (0·15 g.), m. p. 145—147° undepressed on admixture with an authentic specimen of lapachonole picrate. The picrate was dissolved in ether and decomposed by chromatography to give a gum, which on crystallisation from light petroleum (b. p. 40—60°) formed needles (0·03 g.), m. p. 57—59° undepressed on admixture with natural lapachenole [1] (Found : C, 80·2; H, 6·55. $C_{16}H_{14}O_2$ requires C, 80·0; H, 6·65%).

*Lapachenole Dimer.*—A mixture of the crude distillation product (0·2 g.) and formic acid (6 c.c.; s.g. 1·2) was heated on a steam-bath for 1 hr. The mixture was cooled and the precipitate separated by filtration, washed with sodium hydrogen carbonate solution and water, and dried. Crystallisation from ethyl acetate afforded needles (0·1 g.), m. p. 255—256° undepressed on admixture with authentic lapachenole dimer.[1]

*4-Methoxy-1-naphthyl ββ-Dimethylacrylate* (V).—4-Methoxynaphthol (IV) (7 g.), ββ-dimethylacryloyl chloride [10] (8 g.; b. p. 47°/11 mm.), magnesium (0·6 g.), and benzene (60 c.c.) were refluxed for 1 hr. Distillation of the oily *product* gave a fraction (6·55 g.), b. p. 214—215°/4 mm., crystallising in yellowish squat prisms, m. p. 64—65° (Found : C, 74·9; H, 6·4. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%).

*6-Methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-one* (IV).—4-Methoxy-1-naphthyl ββ-dimethylacrylate (6·5 g.) and anhydrous aluminium chloride (8 g.) were heated at 140—150° for 3 hr. Addition of hydrochloric acid (1 : 1; 40 c.c.), isolation with ether–chloroform (4 : 1), and removal of the solvent gave a gum (5·5 g.).

This was extracted with dry methanol (200 c.c.); after filtration the methanolic solution was saturated with dry hydrogen chloride, warmed on a steam-bath for 3 hr., cooled, resaturated with dry hydrogen chloride, and set aside overnight. Water (70 c.c.) was added and the alcohol removed by distillation. The cooled residue was saturated with ammonium sulphate, and the oil dissolved in ether.

Evaporation of solvent gave a gum (4·4 g.), which was boiled with ethanol (130 c.c.) and hydrochloric acid (3%; 100 c.c.) for 24 hr., and then set aside at room temperature for 36 hr. After distillation of ethanol (130 c.c.), the residue was diluted with saturated ammonium sulphate solution. The mixture was extracted with ether (3 × 150 c.c.), and the ethereal solution washed with sodium hydroxide solution, and water. Evaporation of the dried ($CaCl_2$) extract gave a brownish-yellow solid (1·8 g.) which was chromatographed on alumina from benzene solution. Removal of solvent and crystallisation from aqueous ethanol afforded *6-methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-one* as cream needles (1·2 g.), m. p. 120·5—121·5° (Found : C, 74·9; H, 6·2. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%).

*6-Methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-ol* (VI).—6-Methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-one (1 g.) in ether (25 c.c.) was slowly added to an excess of lithium aluminium hydride in ether. The solution was refluxed for 1 hr. and set aside at room temperature for a further 1 hr. After decomposition, the ethereal layer was separated and the aqueous layer extracted with ether after being saturated with ammonium sulphate. The combined ethereal solutions were washed with sodium hydrogen carbonate solution and water. Evaporation of solvent and crystallisation from aqueous ethanol gave fine needles, m. p. 107·5—109° (Found : C, 74·1; H, 6·8. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%).

*Lapachenole* (I).—Acetic anhydride (1 c.c.) was slowly added to a well-cooled solution of *6-methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-ol* (0·35 g.) in pyridine (5 c.c.). After 2 hours at room temperature the solution was poured into ice–hydrochloric acid. The product was isolated with ether and the ethereal solution repeatedly washed with dilute hydrochloric acid. Removal of solvent yielded a gum (0·35 g.) which was heated at 180—190° for 1 hr. at 13—14 mm. in a wide tube fitted with a cooled finger and connected with a cooled trap. An ethereal solution of the distillate and residue was washed with sodium hydrogen carbonate solution and with water. Evaporation of the dried extract gave a brown gum (0·2 g.); addition of a saturated methanolic solution of picric acid and crystallisation from methanol gave dark-violet needles (0·25 g.), m. p. 148—149° undepressed on admixture with authentic lapachenole picrate. The picrate in ether was decomposed by chromatography; the product (0·13 g.) after crystallisation from light petroleum (b. p. 40—60°) had m. p. 57—59°, undepressed on admixture with authentic lapachenole.

*Lapachenole Dimer.*—6-Methoxy-2 : 2-dimethyl-7 : 8-benzochroman-4-ol (0·05 g.) was heated with syrupy phosphoric acid (5 c.c.) at 180° for ¾ hr. The mixture was poured into water and the product extracted with ether. Removal of solvent from the cleaned and dried extract gave a gum (0·01 g.), which was triturated with methanol. Recrystallisation of the product from ethyl acetate gave needles (0·004 g.), m. p. 245—254° undepressed on admixture with authentic lapachenole dimer.

The authors gratefully acknowledge provision of facilities for some of the microanalyses by Professor E. H. R. Jones, F.R.S., at the University of Manchester, and thank Mr. E. S. Morton for these determinations. They also thank Dr. M. C. Whiting for his interest in this work. One (R. B. W.) thanks Burnley Education Authority for financial assistance.

MUNICIPAL COLLEGE, BURNLEY. [*Received, March 27th*, 1956.]

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## 719. *Infrared Spectra and Polar Effects. Part IV.* Steric Restrictions of Polar Effects and their Application in Studies on Rotational Isomerism.*

By L. J. BELLAMY, L. C. THOMAS, and R. L. WILLIAMS.

A halogen atom in the α-position to a carbonyl group does not influence the C=O frequency unless it is close in space to the oxygen atom. This effect is utilised in the differentiation of rotational isomers of a number of derivatives of ω-chloroacetophenone. In each case the more stable isomer is shown to be that in which the chlorine atom is *cis* with respect to the carbonyl group.

THE frequency shifts of mass-insensitive vibrations in the infrared region are, in general, directly related to the inductive and mesomeric effects of the substituents attached to the group concerned.[1,2] However, there are a few anomalous cases which cannot be explained on this basis, one of the most interesting being the observation that the carbonyl frequencies of cyclic ketones show a rise of about 20 cm.$^{-1}$ when an α-halogen atom is introduced equatorially but remain substantially unaffected by an α-halogen atom in the polar position.[3-6] This cannot be reconciled with an inductive effect which should be independent of steric considerations, or with a mesomeric effect which would be expected to lead to a fall in frequency, and we have therefore studied it further. Consideration of the available data on α-halogenated carbonyl compounds suggests that this steric effect is not limited to cyclic compounds, and that in contrast to Gillette's findings [7] it is only the first α-halogen atom which has any major influence upon the carbonyl frequency. This results in an initial

* Part III, *J.*, 1956, 2753.

[1] Bellamy, *J.*, 1955, 2818.
[2] *Idem, ibid.*, p. 4221.
[3] Jones, Ramsey, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1954, **74**, 2828.
[4] Dickson and Page, *J.*, 1955, 447.
[5] Corey, Topie, and Wozniak, *J. Amer. Chem. Soc.*, 1955, **77**, 5415.
[6] Corey and Burke, *ibid.*, p. 5418.
[7] Gillette, *ibid.*, 1936, **58**, 1143.

rise of some 20—30 cm.$^{-1}$, but thereafter further halogen substitution at the same carbon atom either has no effect or results in only small shifts which can be associated with residual inductive effects. Thus the ethyl esters of mono-, di-, and tri-chloro- and bromofluoro-, and chlorofluoro-acetic acid absorb [1,4,8,9] within the range 1761—1753 cm.$^{-1}$ in the liquid state. Similarly, the introduction of an α-fluorine atom into ethyl acetate raises the carbonyl frequency by 27 cm.$^{-1}$ but the difluorinated material absorbs only 4 cm.$^{-1}$ higher, with a further rise of 9 cm.$^{-1}$ in the trifluorinated ester.[10] Recent work on trichloroacetic acid [11] has also shown that in monomeric form this compound has a carbonyl frequency only 18 cm.$^{-1}$ higher than the original acid and this corresponds to the shift which would be expected from the influence of a single chlorine atom. Many other parallel cases can be cited such as the observation that ωω′-dibromoacetophenone-*o*-carboxylic acid has the same carbonyl frequency as the monobromo-derivative,[12] and our own similar results on mono- and di-chloroacetophenones (see below). These findings contrast with the results obtained from compounds containing the group ·CHBr·CO·$CH_2$Br. In these cases it is possible for both the halogen atoms to be near in space or coplanar with the carbonyl group, and the frequency shift shown is then approximately double that of the monosubstituted product.[3]

These results indicate that inductive effects are playing only a relatively small part in the alterations of these carbonyl frequencies and that the major effect is due to some other cause which only becomes effective when the halogen atom is close in space to the carbonyl oxygen. Further, as the introduction of an α-halogen atom into any open-chain structure ·$CH_2$·CO· invariably results in a rise in the carbonyl frequency, it follows that the structure in which the halogen atom is close to the carbonyl oxygen is the preferred stable form. Nevertheless, as rotation is possible about the C–C bond of this group one would expect to find a second carbonyl absorption when such compounds are examined in the liquid or vapour state. This second form would correspond to a rotational isomer in which the chlorine atom was twisted away from the oxygen and the carbonyl frequencies should therefore be unaffected by it; hence, it is satisfying to find that compounds such as bromo-acetic and fluoroacetic ester, in which this effect should be most clearly marked, do in fact exhibit a second C=O absorption in the liquid and solution state which is very close to the carbonyl frequency of acetic ester itself.[8,9] Josien and Calas [13] have noted similar effects in both mono- and di-chlorinated esters and have already suggested that they may be associated with restricted rotation effects.

This finding therefore provides further confirmation of the steric limitation of this effect and suggests a useful application in restricted rotation studies. Mizushima *et al.*[14,15] have studied rotational isomerism in compounds such as bromo- and chloro-acetyl chloride and chloroacetone. They have used dipole-moment and similar studies to differentiate the two configurations but have used infrared data in their recognition. A study of the latter data shows that all these compounds have two carbonyl frequencies in the liquid or vapour state and only one in the crystalline solid. Further, the two frequencies in the liquid state differ by the expected amount of 20—30 cm.$^{-1}$, whilst dipole-moment data, etc., indicate that in every case the more stable isomer is that in which the halogen atom is *cis* with respect to the carbonyl group and therefore close to it in space.

Owing to the frequency shifts in carbonyl absorptions which accompany changes of state, and which themselves amount to as much as 20 cm.$^{-1}$ in the case of acetophenones,[16,17] the frequencies given in various states cannot be compared directly to determine which is

[8] Hampton and Newell, *Analyt. Chem.*, 1949, **12**, 914.
[9] McBee and Christman, *J. Amer. Chem. Soc.*, 1955, **77**, 755.
[10] Bender, *ibid.*, 1953, **75**, 5986.
[11] Fuson, Josien, Jones, and Lawson, *J. Chem. Phys.*, 1952, **20**, 1627.
[12] Grove and Willis, *J.*, 1951, 877.
[13] Josien and Calas, *Compt. rend.*, 1955, **240**, 1641.
[14] Nakagawa, Ichishima, Kuratani, Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1952, **20**, 1720.
[15] Mizushima, Shimanouchi, Miyazawa, Ichishima, Kuratani, Nakagawa, and Shido, *ibid.*, 1953, **21**, 815.
[16] Soloway and Freiss, *J. Amer. Chem. Soc.*, 1951, **73**, 5000.
[17] Fuson, Josien, and Shelton, *ibid.*, 1954, **76**, 2526.

the stable form in the solid. However, the knowledge that the isomer in which the halogen and the carbonyl group are *cis* can be expected to show a carbonyl frequency some 20 cm.$^{-1}$ higher than that in which they are not should enable the more stable rotational isomer to be identified readily by a study of relative intensities of the two carbonyl absorptions of the liquids at a variety of temperatures. This possibility has been explored in the case of a series of derivatives of ω-chloroacetophenone, and the results obtained are given below.

## Experimental

Samples were examined in either a Perkin-Elmer 21 or a Grubb-Parsons S.3A double-beam spectrometer fitted with a rock-salt prism. Solids were examined as pressed discs in potassium bromide and as films pressed between rock-salt plates. Experiments on solutions were carried out in carbon tetrachloride. The liquids and molten films were examined in a conventional hot cell of the type described by Richards and Thompson.[18] The spectra of the liquids were run at a stepwise series of temperatures above the m. p. and changes in the relative intensities of the two carbonyl absorptions were recorded.

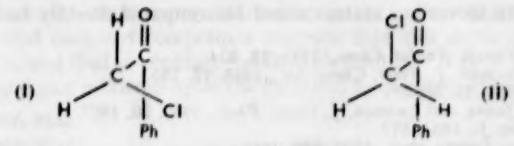
*Results.*—The compounds studied and the results obtained are listed in the Table. The relative intensity changes with temperature of the two carbonyl frequencies of one typical compound—ω : 3 : 4-trichloroacetophenone—are illustrated in the Figure.

*Carbonyl frequencies (cm.$^{-1}$) of ω-chloroacetophenone derivatives in various states.*

| | | | | Effect of rising temperature on liquid : | |
|---|---|---|---|---|---|
| Acetophenone | Solid | Liquid | Solution | C=O intensity grows | C=O intensity falls |
| ω-Chloro- ..... | — | 1697, 1685 | 1704, 1682 | 1685 | 1697 |
| ω : 4-Dichloro- ..... | 1684 | 1695, 1683 | 1704, 1684 | 1683 | 1695 |
| ω : 3 : 4-Trichloro- ..... | 1699 | 1695, 1681 | 1706, 1686 | 1681 | 1695 |
| ω : 2 : 5-Trichloro- ..... | 1706 | 1718, 1703 | 1724, 1704 | 1703 | 1718 |
| ω : 2 : 4-Trichloro- ..... | 1701 | 1706, 1694 | 1721, 1701 | 1694 | 1706 |
| ω : 2 : 4 : 6-Tetrachloro- | 1727 | 1730, 1711 | 1733, 1715 | 1711 | 1730 |
| ωω-Dichloro- ..... | — | 1698, 1684 | 1701, 1681 | 1684 | 1698 |

These results raise a number of interesting points. The occurrence of a single C=O frequency in the solids and of two in the liquids is clear evidence for the existence of rotational isomerism in these compounds. In ω-chloroacetophenone, one of the two carbonyl bands shown in the liquid state occurs at precisely the same frequency as the carbonyl absorption of liquid acetophenone (1682 cm.$^{-1}$) whilst the other absorbs 12 cm.$^{-1}$ higher. In the light of the above discussion, the 1682 cm.$^{-1}$ band must be associated with the form (I) in which the chlorine atom is twisted away from the carbonyl group and does not therefore affect its frequency. Similarly, the 1697 cm.$^{-1}$ band must correspond to the form (II) in which the oxygen and the chlorine atom are close together.

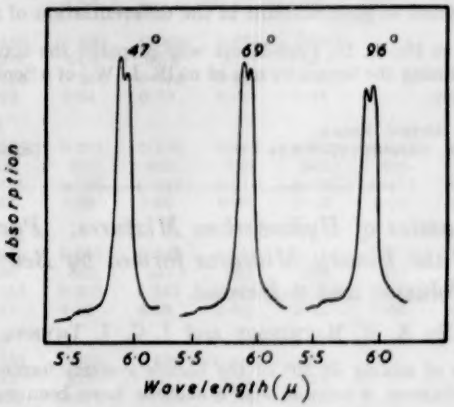
Very similar results are given by the 4-chloro- and the 3 : 4-dichloro-derivative. However, when a further chlorine atom is introduced into the 2-position of the ring a further small frequency rise is shown by both the carbonyl frequencies of the liquid forms. This could be due to a small degree of twisting of the chloroacetyl group out of the plane of the ring, but it is perhaps more likely to be associated with a direct effect upon the carbonyl group of the ring-chlorine atom. This is also very close in space to the carbonyl oxygen atom and could therefore influence its frequency in the same way as an α-halogen substituent. In one configuration,




therefore, the carbonyl group would come under the influence of two halogen atoms whilst in the other only the ring-halogen would exert any effect. In the case of the 2 : 4 : 6-trichloro-derivative it is clear from molecular models that the introduction of halogen atoms on each side of

[18] Richards and Thompson, *Trans. Faraday Soc.*, 1945, **41**, 183.

the chloroacetyl group compels the latter to rotate out of the plane of the ring. Two configurations of this group are possible, as before, but in neither of these is the ring coplanar with the carbonyl group, and the frequencies of both rise sharply owing to the elimination of the mesomeric effect of the ring.




The detailed study of the relative intensities of the two carbonyl absorptions of each of the liquids fully confirms the expectation that the form in which the chlorine atom is *cis* with respect to the carbonyl group is the more stable one. The results shown in the Figure are typical of all the cases studied, and it will be seen that as the temperature is raised the proportion of the form giving rise to the lower carbonyl band is increased. From the data given earlier this is clearly the form in which the halogen atom and the carbonyl group are not *cis*, which is accordingly the less stable isomer.

It would also have been interesting to study the C–Cl absorptions of these isomers. Mizushima *et al.*[14,15] have found that in all the cases in which the halogen atom is *cis* with respect to the carbonyl oxygen, the C–Cl frequency also rises. This is indirectly confirmed by McBee and Christman [7] who find a similar effect in chlorinated esters. However, in the present series the occurrence of a number of absorptions in the expected region, coupled with the low intensities of the C–Cl bands and the presence of other C–Cl frequencies in many cases, has rendered any reasonable identification of these bands impracticable.

## Discussion

These findings show that the existence of a steric factor in determining whether or not an α-halogen substituent will raise a carbonyl frequency is very real. Also, this effect must have some stabilising power, since, despite the steric repulsions which might be expected between the chlorine and oxygen atoms, the stable form of all the compounds studied is that in which these atoms approach as closely together as possible. This holds also for the compounds studied by Mizushima [14,15] and it can be deduced from the high carbonyl frequencies of halogenated esters that they also take up this preferred orientation. Furthermore, as has been indicated above, there is evidence that in many cases the C–Cl frequency is also increased when the chloro-group is *cis* to the carbonyl group. The apparent strengthening of both the C=O and C–Cl bands in this orientation points to some form of resonance stabilisation, but this cannot be a normal mesomeric effect, which would lead to a fall in the carbonyl frequency owing to an increase in the proportion of the polar form $\rangle\overset{+}{C}-\overset{-}{O}$. A very similar situation appears to arise in acid chlorides in which both the C=O and C–Cl links appear to be strengthened, and it is perhaps noteworthy that both these instances differ sharply from the behaviour of the corresponding vinyl compounds. Thus the substitution of a trifluoromethyl group in the α-position to a C=C bond has little or no effect upon the C=C frequency,[19] whilst in vinyl chloride the C=C frequency is actually lowered, through the operation of a normal mesomeric effect.

[19] Haszeldine, *Nature*, 1951, **168**, 1028.

The origins of this effect are still obscure and we intend to study other related anomalous cases in the hope that some common factor may emerge. It is, however, clear that an electrical effect which is neither an inductive nor a mesomeric effect is operating in the case of α-halogenated carbonyl compounds, and that this effect is subject to a steric limitation which can be turned to good account in the differentiation of rotational isomers.

Thanks are offered to Mr. A. H. Ford-Moore who prepared the compounds studied. This work was carried out during the tenure by one of us (R. L. W.) of a Senior Research Fellowship of the Ministry of Supply.

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## 720. *Thermodynamics of Hydrocarbon Mixtures. Part II.* The Heats of Mixing of the Binary Mixtures formed by Benzene, cyclo*Hexane, n-*Heptane, Toluene, and* n-*Hexane.*

By A. R. Mathieson and J. C. J. Thynne.

The heats of mixing at 20° of the binary systems formed by benzene, toluene, *cyclo*hexane, *n*-hexane, and *n*-heptane have been measured. The volume changes on mixing have also been measured for most of these systems. From these data, values have been calculated for solubility parameters and interaction parameters, and these values are considered in terms of the theories of liquid mixtures. Kirkwood's equation to correct for non-uniform distribution of molecules in a mixture has been found to be in good agreement with the results.

The heats of mixing at 20° have been measured for seven binary mixtures formed by benzene, *cyclo*hexane, *n*-heptane, toluene, and *n*-hexane, the other three pairs having been reported in Part I. The volumes of mixing at 25° have also been measured for several of these binary mixtures.

### Experimental

The volumes of mixing were measured by means of a single-stem pycnometer, which was fitted with a B7 joint and stopper to prevent evaporation. The technique involved was similar to that of previous workers.[1,2] The heats of mixing were measured as described in Part I.

*Purity of Materials.—Toluene.* B.P. grade was shaken repeatedly with concentrated sulphuric acid, washed with aqueous sodium carbonate, then water, and dried ($CaCl_2$). It was fractionated through a 1½ m. column packed with glass helices, and the fraction of boiling range 110·58—110·62° collected.

n-*Hexane.*[3] The spectroscopic grade was shaken at 45° with redistilled chlorosulphonic acid, washed with concentrated sulphuric acid, water, 10% sodium hydroxide solution, and water, and dried ($CaCl_2$). The fraction collected had b. p. 68·40°.

Benzene, *cyclo*hexane, and *n*-heptane were purified as described in Part I.

The properties of the first two liquids are summarised below, values reported by Rossini *et al.*[4] being given in parentheses.

| | B. p. (760 mm.) | $n_D^{25}$ | $d_4^{25}$ |
|---|---|---|---|
| Toluene | 110·60° (110·623°) | 1·4940 (1·49405) | 0·86121 (0·86220) |
| *n*-Hexane | 68·40 (68·742) | 1·3738 (1·37226) | 0·65892 (0·65481) |

### Results

For convenience, the five hydrocarbons are allotted subscripts: benzene, 1; *cyclo*hexane, 2; *n*-heptane, 3; toluene, 4; *n*-hexane, 5. Then $\Delta H_{14}$ is the heat of mixing per mole of the mixture

* Part I, *J.*, 1955, 4141.

[1] Wood and Brasie, *J. Amer. Chem. Soc.*, 1943, **65**, 1891.
[2] Wood and Austin, *ibid.*, 1945, **67**, 480.
[3] Shepard, Midgely, and Henne, *ibid.*, 1931, **53**, 1948.
[4] Rossini, *J. Res. Nat. Bur. Stand.*, 1946, **36**, 129.

benzene and toluene, and $x_1$, $\phi_1$ are the mole fraction and volume fraction of benzene. Table 1 shows the heat of mixing of seven of the ten possible binary mixtures; the results for the other three binary mixtures have been given in Part I.

TABLE 1. *Heats of mixing at 20°.*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ***Benzene–Toluene*** ($\Delta H_{14}$) | | | | | | | | | |
| $x_1$ | 0·199 | 0·390 | 0·560 | 0·665 | 0·780 | | | | |
| $\Delta H_{14}$ (J/mole) | 43·5 | 64·0 | 67·8 | 61·5 | 48·1 | | | | |
| $\phi_1$ | 0·175 | 0·348 | 0·514 | 0·624 | 0·748 | | | | |
| $\Delta H_{14}$ (J/ml.) | 0·42 | 0·64 | 0·70 | 0·65 | 0·51 | | | | |
| ***Benzene–n-Hexane*** ($\Delta H_{15}$) | | | | | | | | | |
| $x_1$ | 0·175 | 0·301 | 0·310 | 0·403 | 0·470 | 0·563 | 0·667 | 0·788 | 0·866 |
| $\Delta H_{15}$ (J/mole) | 452 | 657 | 669 | 795 | 841 | 866 | 837 | 628 | 469 |
| $\phi_1$ | 0·128 | 0·229 | 0·238 | 0·318 | 0·385 | 0·471 | 0·581 | 0·720 | 0·818 |
| $\Delta H_{15}$ (J/ml.) | 3·64 | 5·56 | 5·69 | 6·99 | 7·49 | 8·08 | 8·12 | 6·40 | 4·94 |
| cyclo***Hexane–Toluene*** ($\Delta H_{24}$) | | | | | | | | | |
| $x_2$ | 0·250 | 0·300 | 0·340 | 0·435 | 0·516 | 0·570 | 0·708 | 0·733 | |
| $\Delta H_{24}$ (J/mole) | 460 | 523 | 531 | 590 | 594 | 611 | 536 | 485 | |
| $\phi_2$ | 0·253 | 0·303 | 0·344 | 0·438 | 0·520 | 0·573 | 0·711 | 0·736 | |
| $\Delta H_{24}$ (J/ml.) | 4·27 | 4·85 | 4·98 | 5·48 | 5·52 | 5·65 | 4·94 | 4·48 | |
| n-***Heptane–Toluene*** ($\Delta H_{34}$) | | | | | | | | | |
| $x_3$ | 0·220 | 0·395 | 0·498 | 0·648 | 0·658 | | | | |
| $\Delta H_{34}$ (J/mole) | 397 | 531 | 561 | 498 | 498 | | | | |
| $\phi_3$ | 0·279 | 0·473 | 0·576 | 0·717 | 0·727 | | | | |
| $\Delta H_{34}$ (J/ml.) | 3·77 | 4·44 | 4·31 | 3·68 | 3·72 | | | | |
| cyclo***Hexane–n-Hexane*** ($\Delta H_{25}$) | | | | | | | | | |
| $x_2$ | 0·254 | 0·275 | 0·290 | 0·301 | 0·499 | 0·511 | 0·615 | 0·810 | 0·835 |
| $\Delta H_{25}$ (J/mole) | 119 | 145 | 138 | 145 | 215 | 220 | 211 | 149 | 126 |
| $\phi_2$ | 0·223 | 0·242 | 0·258 | 0·267 | 0·457 | 0·468 | 0·574 | 0·782 | 0·810 |
| $\Delta H_{25}$ (J/ml.) | 0·95 | 1·16 | 1·11 | 1·17 | 1·80 | 1·84 | 1·80 | 1·32 | 1·12 |
| ***Toluene–n-Hexane*** ($\Delta H_{45}$) | | | | | | | | | |
| $x_4$ | 0·254 | 0·290 | 0·320 | 0·477 | 0·522 | 0·614 | 0·785 | | |
| $\Delta H_{45}$ (J/mole) | 360 | 402 | 427 | 456 | 469 | 427 | 326 | | |
| $\phi_4$ | 0·218 | 0·253 | 0·278 | 0·430 | 0·472 | 0·567 | 0·740 | | |
| $\Delta H_{45}$ (J/ml.) | 2·89 | 3·26 | 3·47 | 3·81 | 3·93 | 3·68 | 2·93 | | |
| n-***Heptane–n-Hexane*** ($\Delta H_{35}$) | | | | | | | | | |
| $x_3$ | 0·396 | 0·420 | 0·720 | 0·821 | | | | | |
| $\Delta H_{35}$ (J/mole) | 15·5 | 23·4 | 9·2 | 5·0 | | | | | |
| $\phi_3$ | 0·428 | 0·459 | 0·765 | 0·839 | | | | | |
| $\Delta H_{35}$ (J/ml.) | 0·11 | 0·17 | 0·06 | 0·03 | | | | | |

The volumes of mixing are shown in Table 2; $\Delta V_{14}$ is the volume change per mole of mixture, and $V_0 = x_1V_1 + x_4V_4$, where $V_1$ and $V_4$ are the molar volumes of the pure components at 25°.

TABLE 2. *Volumes of mixing at 25°.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ***Benzene–Toluene*** ($\Delta V_{14}$) | | | | ***Benzene–n-Hexane*** ($\Delta V_{15}$) | | | | | | |
| $x_1$ | 0·446 | 0·557 | 0·604 | $x_1$ | 0·266 | 0·325 | 0·567 | 0·576 | 0·588 | 0·834 |
| $100\Delta V_{14}/V_0$ | 0·152 | 0·148 | 0·140 | $100\Delta V_{15}/V_0$ | 0·255 | 0·289 | 0·433 | 0·433 | 0·422 | 0·315 |
| $\phi_1$ | 0·402 | 0·512 | 0·560 | $\phi_1$ | 0·204 | 0·250 | 0·475 | 0·486 | 0·497 | 0·777 |
| cyclo***Hexane–Toluene*** ($\Delta V_{24}$) | | | | ***Toluene–n-Hexane*** ($\Delta V_{45}$) | | | | ***Toluene–n-Heptane*** ($\Delta V_{47}$) | | |
| $x_2$ | 0·416 | 0·571 | | $x_4$ | 0·401 | | | $x_4$ | 0·477 | 0·510 |
| $\phi_2$ | 0·420 | 0·576 | | $\phi_4$ | 0·357 | | | $\phi_4$ | 0·555 | 0·586 |
| $100\Delta V_{24}/V_0$ | 0·546 | 0·550 | | $100\Delta V_{45}/V_0$ | 0·221 | | | $100\Delta V_{47}/V_0$ | 0·193 | 0·189 |
| cyclo***Hexane–n-Hexane*** ($\Delta V_{25}$) | | | | cyclo***Hexane–n-Heptane*** ($\Delta V_{27}$) | | | | ***Benzene–n-Heptane*** ($\Delta V_{17}$) | | |
| $x_2$ | 0·433 | 0·528 | 0·673 | $x_2$ | 0·501 | 0·590 | | $x_1$ | 0·430 | 0·604 | 0·813 |
| $\phi_2$ | 0·392 | 0·486 | 0·636 | $\phi_2$ | 0·426 | 0·516 | | $\phi_1$ | 0·314 | 0·481 | 0·725 |
| $100\Delta V_{25}/V_0$ | 0·182 | 0·198 | 0·168 | $100\Delta V_{27}/V_0$ | 0·261 | 0·274 | | $100\Delta V_{17}/V_0$ | 0·479 | 0·521 | 0·449 |
| ***Benzene–cyclo**Hexane* ($\Delta V_{12}$) | | | | | | | | | | |
| $x_1$ | 0·175 | 0·242 | 0·254 | 0·339 | 0·462 | 0·475 | 0·508 | 0·512 | | |
| $\phi_1$ | 0·148 | 0·208 | 0·219 | 0·296 | 0·414 | 0·426 | 0·459 | 0·464 | | |
| $100\Delta V_{12}/V_0$ | 0·368 | 0·436 | 0·462 | 0·618 | 0·633 | 0·631 | 0·633 | 0·654 | | |
| $x_1$ | 0·559 | 0·577 | 0·580 | 0·620 | 0·769 | 0·808 | 0·860 | 0·881 | | |
| $\phi_1$ | 0·508 | 0·529 | 0·532 | 0·573 | 0·732 | 0·776 | 0·835 | 0·859 | | |
| $100\Delta V_{12}/V_0$ | 0·648 | 0·651 | 0·664 | 0·611 | 0·506 | 0·546 | 0·329 | 0·298 | | |

The results for the heats and volumes of mixing (Tables 1 and 2) are best represented by the following equations :

*Benzene–Toluene*

$$\Delta H_{14} = x_1x_4[272 - 18{\cdot}8(x_1 - x_4) - 5{\cdot}4(x_1 - x_4)^2] \quad (1)$$
$$\Delta H_{14} = \phi_1\phi_4[2{\cdot}76 - 0{\cdot}04(\phi_1 - \phi_4) + 0{\cdot}04(\phi_1 - \phi_4)^2] \quad (2)$$

*Benzene–*n*-Hexane*

$$\Delta H_{15} = x_1x_5[3431 + 781(x_1 - x_5) + 245(x_1 - x_5)^2] \quad (3)$$
$$\Delta H_{15} = \phi_1\phi_5[32{\cdot}60 + 1{\cdot}12(\phi_1 - \phi_5) + 1{\cdot}12(\phi_1 - \phi_5)^2] \quad (4)$$
$$100\Delta V_{15}/V_0 = x_1x_5[1{\cdot}66 + 0{\cdot}80(x_1 - x_5) + 0{\cdot}07(x_1 - x_5)^2] \quad (5)$$
$$100\Delta V_{15}/V_0 = \phi_1\phi_5[1{\cdot}72 + 0{\cdot}23(\phi_1 - \phi_5) + 0{\cdot}10(\phi_1 - \phi_5)^2] \quad (6)$$

cyclo*Hexane–Toluene*

$$\Delta H_{24} = x_2x_4[2385 - 201(x_2 - x_4) - 212(x_2 - x_4)^2] \quad (7)$$
$$\Delta H_{24} = \phi_2\phi_4[22{\cdot}13 + 0{\cdot}08(\phi_2 - \phi_4) + 3{\cdot}61(\phi_2 - \phi_4)^2] \quad (8)$$

*n-Heptane–Toluene*

$$\Delta H_{34} = x_3x_4[2218 - 44{\cdot}8(x_3 - x_4) + 145(x_3 - x_4)^2] \quad (9)$$
$$\Delta H_{34} = \phi_3\phi_4[17{\cdot}4 + 1{\cdot}8(\phi_3 - \phi_4) + 3{\cdot}6(\phi_3 - \phi_4)^2] \quad (10)$$

cyclo*Hexane–*n*-Hexane*

$$\Delta H_{25} = x_2x_5[862 + 279(x_2 - x_5) - 256(x_2 - x_5)^2] \quad (11)$$
$$\Delta H_{25} = \phi_2\phi_5[7{\cdot}36 + 1{\cdot}34(\phi_2 - \phi_5) - 1{\cdot}76(\phi_2 - \phi_5)^2] \quad (12)$$

*Toluene–*n*-Hexane*

$$\Delta H_{45} = x_4x_5[1841 - 123(x_4 - x_5) + 201(x_4 - x_5)^2] \quad (13)$$
$$\Delta H_{45} = \phi_4\phi_5[15{\cdot}41 - 0{\cdot}04(\phi_4 - \phi_5) + 4{\cdot}01(\phi_4 - \phi_5)^2] \quad (14)$$

*n-Heptane–*n*-Hexane*

$$\Delta H_{35} = x_3x_5(62{\cdot}8) \quad (15)$$
$$\Delta H_{35} = \phi_3\phi_5(0{\cdot}33) \quad (16)$$

*Benzene–*n*-Heptane*

$$\Delta H_{13} = \phi_1\phi_3[33{\cdot}81 + 0{\cdot}67(\phi_1 - \phi_3) + 1{\cdot}34(\phi_1 - \phi_3)^2] \quad (17)$$
$$100\Delta V_{13}/V_0 = x_1x_3[2{\cdot}03 + 0{\cdot}82(x_1 - x_3) + 0{\cdot}57(x_1 - x_3)^2] \quad (18)$$
$$100\Delta V_{13}/V_0 = \phi_1\phi_3[2{\cdot}11 + 0{\cdot}05(\phi_1 - \phi_3) + 0{\cdot}72(\phi_1 - \phi_3)^2] \quad (19)$$

*Benzene–*cyclo*Hexane*

$$\Delta H_{12} = \phi_1\phi_2[33{\cdot}53 + 3{\cdot}81(\phi_1 - \phi_2) - 3{\cdot}59(\phi_1 - \phi_2)^2] \quad (20)$$
$$100\Delta V_{12}/V_0 = x_1x_2[2{\cdot}57 + 0{\cdot}34(x_1 - x_2) + 0{\cdot}26(x_1 - x_2)^2] \quad (21)$$
$$100\Delta V_{12}/V_0 = \phi_1\phi_2[2{\cdot}56 - 0{\cdot}26(\phi_1 - \phi_2) + 0{\cdot}34(\phi_1 - \phi_2)^2] \quad (22)$$

cyclo*Hexane–n-Heptane*

$$\Delta H_{23} = \phi_2\phi_3[8{\cdot}87 + 0{\cdot}21(\phi_2 - \phi_3) - 2{\cdot}0(\phi_2 - \phi_3)^2] \quad (23)$$
$$100\Delta V_{23}/V_0 = x_2x_3[1{\cdot}07 + 0{\cdot}22(x_2 - x_3) + 0{\cdot}18(x_2 - x_3)^2] \quad (24)$$
$$100\Delta V_{23}/V_0 = \phi_2\phi_3[1{\cdot}09 + 0{\cdot}12(\phi_2 - \phi_3) - 0{\cdot}27(\phi_2 - \phi_3)^2] \quad (25)$$

## Discussion

The results for $\Delta H_m$ and $100\ \Delta V/V_0$ can always be represented in terms of a power series (equations 1—25), in every case no more than three terms being required to express the results satisfactorily. For *n*-heptane–*n*-hexane the first term only is needed to represent the results to the degree of accuracy obtainable for this system.

It has been found that where the molar volumes of the components of the binary mixture differ by less than 10%, the experimental results generally fall on a curve with its maximum at, or very near to, 0·5, when plotted with respect to mole fraction or to volume fraction. However, where the molar volumes differ considerably the position of the maximum value alters in the case of mole fraction, but remains near to 0·5 for the volume fraction plots, and this is especially noticeable in the case of benzene–*n*-hexane and

TABLE 3.

| System | (a) *Solubility parameters* $\Delta\delta$ (from $\Delta H_m$) | $\Delta\delta$ (from $\Delta E_m^V$) | $\Delta\delta$ (from H. & S.) | (b) *Interaction parameters* $\Delta H/x_1x_2$ | $\Delta V/x_1x_2$ | $d_{12}$ (from $\Delta H$) | $d_{12}$ (from $\Delta V$) |
|---|---|---|---|---|---|---|---|
| Benzene–Toluene ..... | 0·82 | 0·54 | 0·25 | 65 | 0·60 | −0·0080 | −0·0107 |
| Benzene–*cyclo*Hexane ... | 2·85 | 2·46 | 0·95 | 800 | 2·57 | −0·0983 | −0·0714 |
| Benzene–*n*-Hexane ..... | 2·78 | 2·50 | 1·85 | 820 | 1·66 | −0·1007 | −0·0415 |
| Benzene–*n*-Heptane ..... | 2·84 | 2·44 | 1·70 | 918 | 2·03 | −0·1128 | −0·0477 |
| Toluene–*n*-Hexane ..... | 1·94 | 1·66 | 1·60 | 440 | +ve * | −0·0482 | −ve * |
| Toluene–*n*-Heptane ..... | 2·07 | 1·58 | 1·45 | 530 | 0·93 | −0·0581 | −0·0204 |
| Toluene–*cyclo*Hexane ... | 2·29 | 1·96 | 0·70 | 570 | 2·20 | −0·0625 | −0·0574 |
| *cyclo*Hexane–*n*-Hexane ... | 1·32 | 1·13 | 0·90 | 206 | 0·78 | −0·0259 | −0·0182 |
| *cyclo*Hexane–*n*-Heptane | 1·46 | 1·26 | 0·75 | 268 | 1·09 | −0·0337 | −0·0242 |
| *n*-Heptane–*n*-Hexane ... | 0·33 | 0·26 | 0·15 | 15 | — | −0·0020 | — |
| Benzene–Carbon tetrachloride ..... | 1·06 | 0·91 | 0·55 | 100 | 0·06 | −0·0122 | −0·0017 |

* Since only one value of the volume of mixing was observed for this system, no value could be calculated for $\Delta V/x_1x_2$ when $x_1 = 0·5$. The only conclusion that may be drawn is that, since a volume increase occurs on mixing, then the sign of the interaction parameter will be negative. This is of the same sign as that of the parameter calculated from $\Delta H/x_1x_2$.

benzene–*n*-heptane where the molar volumes of the components in each mixture differ by about 40% and 50% respectively.

The energy of vaporisation per millilitre is a factor which has an important rôle in Hildebrand's theory of regular mixtures. The relation is expressed by the equation

$$\delta_1 = (\Delta E_1/V_1)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (26)$$

where $\delta_1$ is called the solubility parameter, $\Delta E_1$ is the energy of vaporisation, and $V_1$ is the molar volume of component 1. Also

$$\Delta\delta_{12} = \delta_1 - \delta_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (27)$$

The factor $\Delta\delta_{12}$ can be calculated from a knowledge of the heat of mixing of the binary mixture 1, 2. This, however, assumes that the heat of mixing at constant pressure ($\Delta H_m$) is equivalent to the energy of mixing at constant volume ($\Delta E_m^V$). Because of the volume change frequently observed on mixing, this relation between the heat of mixing and the energy of mixing is not strictly true. Scatchard,[5] by considering mixing to be a two-step process involving (i) the mixing of the two components at constant volume followed by (ii) expansion (or contraction) of the mixture to return to its original internal pressure, and Hildebrand and Scott,[6] by means of a Taylor expansion series, have related the thermodynamic functions at constant pressure to those at constant volume. Both obtain, to a first approximation, the equation

$$\Delta H_m = \Delta E_m^V (1 + \alpha T) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (28)$$

where $\alpha$ is the coefficient of thermal expansion.

For many liquids at room temperature ($T \sim 300°$ K), $\alpha$ is about $1·2 \times 10^{-3}$, so that

$$\Delta H_m \approx 1·36\Delta E_m^V \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (29)$$

This represents a substantial correction that has to be made to $\Delta H_m$ when calculating the quantity $\Delta\delta_{12}$ by means of Scatchard's equation :[7]

$$\Delta E_m/(x_1V_1 + x_2V_2) = \phi_1(1 - \phi_1)(\Delta\delta_{12})^2 \quad . \quad . \quad . \quad . \quad . \quad (30)$$

Table 3(a) shows values of $\Delta\delta$ calculated (i) from $\Delta H_m$ data, (ii) from $\Delta E_m^V$ by use of equation (30), (iii) from values of the individual solubility parameters at 25° calculated by Hildebrand and Scott.[8] It can be seen that agreement between the calculated values of $\Delta\delta$ and the experimental values is much improved when equation (29) is used but, even so,

[5] Scatchard, *Trans. Faraday Soc.*, 1937, **33**, 160.
[6] Hildebrand and Scott, "The Solubility of Non-electrolytes," Reinhold, New York, 1950, 136.
[7] Scatchard, *Chem. Rev.*, 1931, **8**, 321.
[8] Hildebrand and Scott, *ibid.*, p. 436.

agreement is poor generally. In every case the experimental value of $\Delta\delta$ is higher than the calculated value, in agreement with the results of Vold,[9] Cheesman and Whitaker,[10] and Cheesman and Canning.[11]

For the ten systems studied, only in one case, that of benzene (1), toluene (2), and *cyclo*-hexane (3), does the relation (31) hold to better than 5%. For the other systems, up to 50% deviation from equation (31) is observed. This is in accord with the results of Cheesman and Whitaker, and of Cheesman and Canning, but not with those of Vold.

$$\Delta\delta_{13} = \Delta\delta_{23} + \Delta\delta_{12} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (31)$$

By means of the theory of conformal solutions developed by Longuet-Higgins,[12] the thermodynamic properties of this type of solution can be calculated in terms of the thermodynamic properties of one of the pure components and a difference function. In this theory, which is based upon no definite model for the liquid state, a binary solution may be characterised by only one parameter, the difference function $d_{12}$.

The difference function (or the interaction parameter) $d_{12}$ may be calculated separately

FIG. 1.

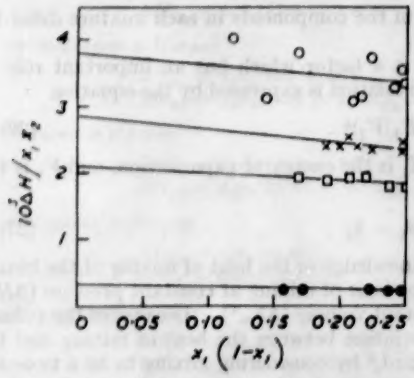
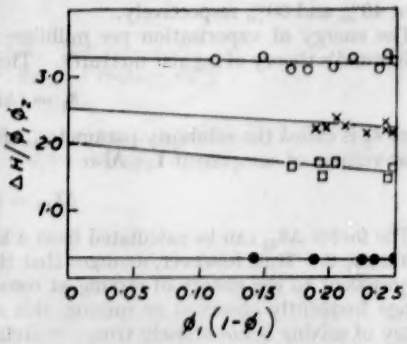



FIG. 2.




○, Benzene–*n*-Hexane. ×, *cyclo*Hexane–Toluene. □, Toluene–*n*-Hexane. ●, Benzene–Toluene.

from heat-of-mixing data, and from volume-of-mixing data, by means of equations (32) and (33). This affords a means of comparison of the values of the parameter when calculated from two sources :

$$d_{12} = \Delta H/x_1x_2(T \cdot dE_0/dT - E_0) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (32)$$

$$d_{12} = \Delta V/[x_1x_2(-T\alpha_0) \cdot V_0^1] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (33)$$

where $V_0^1$ = molar volume, $\alpha_0$ = coefficient of thermal expansion and $E_0$ = latent heat of vaporisation of either of the pure components.

The values obtained for the interaction parameter $d_{12}$, calculated from both sets of data, are given in Table 3(b). In every case the sign of the parameter is the same whether calculated from $\Delta H_m$ or from $\Delta V_m$, and the values are approximately of the same magnitude. The actual numerical differences are relatively unimportant, since $d_{12}$ represents the difference between quantities close to unity.

Prigogine and Mathot [13] have recently developed a theory of solutions based upon a lattice model, where the mean cell-field is represented by a smoothed potential, that is, by

[9] Vold, *J. Amer. Chem. Soc.*, 1937, **59**, 1515.
[10] Cheesman and Whitaker, *Proc. Roy. Soc.*, 1952, *A*, **212**, 406.
[11] Cheesman and Canning, *J.*, 1955, 1230.
[12] Longuet-Higgins, *Proc. Roy. Soc.*, 1951, *A*, **205**, 247.
[13] Prigogine and Mathot, *J. Chem. Phys.*, 1952, **20** 49.

a potential well with a flat base and vertical walls. By this means, equations may be obtained to express the thermodynamic functions in terms of three parameters $\Lambda_{11}$, $\Lambda_{12}$, and $\Lambda_{22}$ which are measures of the intermolecular attractions and are related to the molecular energies of vaporisation. In this treatment an equation may be obtained for the excess volume of mixing. This equation predicts that when $\Lambda_{12} = (\Lambda_{11}\Lambda_{22})^{\frac{1}{2}}$ then a contraction will be observed when components 1 and 2 are mixed. No contractions on mixing have been observed in this work, although several such cases have been reported.[14,15]

The series expansion derived by Kirkwood [16] to correct for the non-uniform distribution of the molecules in a mixture can be reduced to the following form if the higher terms are neglected :

$$\frac{\Delta H_m}{x(1-x)} = \frac{Nw}{z}\left[1 - \frac{x(1-x)w}{kT}\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (34)$$

where $N$ is Avogadro's number, $z$ is the co-ordination number of the quasi-lattice, and $w$ is the interchange energy. The experimental results have been plotted so as to test this equation and in most cases an excellent linear relation is observed between $\Delta H_m/x(1-x)$ and $x(1-x)$. In cases where there is a scatter of the experimental points (always in cases where the molar volumes of the components differ appreciably), then representation of the results is very much improved by plotting $\Delta H/\phi_1(1-\phi_1)$ against $\phi_1(1-\phi_1)$. This is extremely well illustrated for the mixture benzene–*n*-hexane, Figs. 1 and 2 showing some of these results.

Values of $\Delta H/x_1x_2$ in Table 3(b) represent the values of the interchange energies of the binary mixtures expressed in calories per mole of mixture.

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THE UNIVERSITY, NOTTINGHAM. [*Received, March 28th*, 1956.]

[14] Mathot and Desmyter, *J. Chem. Phys.*, 1953, **21**, 782.
[15] Rowlinson and Thacker, *ibid.*, p. 2242.
[16] Kirkwood, *ibid.*, 1938, **6**, 70.

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## 721. *Thermodynamics of Hydrocarbon Mixtures. Part III.* The Heats of Mixing of Ternary, Quaternary, and Quinary Mixtures formed by Benzene, cycloHexane, Heptane, Toluene, and Hexane.*

By A. R. MATHIESON and J. C. J. THYNNE.

The heats of mixing of ternary, quaternary, and quinary systems formed by benzene, toluene, *cyclo*hexane, hexane, and heptane have been measured at 20° C in order to examine various equations which enable the heats of mixing of multicomponent mixtures to be predicted from a knowledge of the heats of mixing of the constituent binary mixtures. It has been found that values agreeing to within the limit of experimental error with those measured may be predicted by some of these equations. An empirical equation has also been suggested.

BY using the method described in Part I,[1] the heats of mixing of multicomponent hydrocarbon mixtures have been measured. For quaternary and quinary mixtures a known amount of a binary mixture, which was contained in the sealed glass ampoule, was mixed with a known amount of a second binary (or ternary) mixture, and the heat of mixing was measured. Since the heats of mixing for both of the mixtures were known at the concentrations used, the total heat of mixing for the multicomponent mixture could be determined.

* Part II, preceding paper.
[1] Part I, *J.*, 1955, 4141.

Since this technique involved two sets of concentration determinations, together with errors in the measurement of temperature and in extrapolation, the estimated experimental error is larger than the error involved in work on binary mixtures, and the percentage errors are estimated as ±3% for ternary systems, ±5% for quaternary systems, and about ±6% for quinary systems.

## Results

*Properties of the Materials.*—These were the same as for the liquids described in Parts I and II.[1,2]

*Heats of Mixing at 20° c.*—In Tables 1—9 the subscript numerals given to $x$ correspond to the order of citation of compounds in the Table heading. $\Delta H_m$ is expressed in J/mole throughout.

## Discussion

Tables 1—9 show the results for the heats of mixing at 20° c of six of the ternary mixtures, two of the quaternary mixtures, and the quinary mixture formed by benzene, toluene, *cyclo*hexane, hexane, and heptane. The results for the ternary mixture, benzene–*cyclo*hexane–heptane have already been reported.[1]

Several equations have been suggested to enable the heats of mixing of multicomponent systems to be predicted from the heats of mixing of the constituent binary mixtures.

That suggested by Redlich and Kister [3] can be expressed for a ternary mixture as :

$$\begin{aligned}\Delta H_{123} = {} & x_1^1 x_2^1[H_{12}^{\circ} + H_{12}^1(x_1^1 - x_2^1) + H_{12}^{11}(x_1^1 - x_2^1)^2 \ldots] \\ & + x_2^1 x_3^1[H_{23}^{\circ} + H_{23}^1(x_2^1 - x_3^1) + H_{23}^{11}(x_2^1 - x_3^1)^2 \ldots] \\ & + x_1^1 x_3^1[H_{13}^{\circ} + H_{13}^1(x_1^1 - x_3^1) + H_{13}^{11}(x_1^1 - x_3^1)^2 \ldots] \quad . \quad (1)\end{aligned}$$

where $H_{12} = x_1 x_2[H_{12}^{\circ} + H_{12}^1(x_1 - x_2) + H_{12}^{11}(x_1 - x_2)^2 \ldots]$ etc. and $x_1^1$, $x_2^1$, and $x_3^1$ are the ternary mole fractions and $x_1$, $x_2$ the binary.

For a quaternary mixture, eqn. 1 will consist of six terms involving the binary equations, and for the quinary mixture there will be ten such terms.

Eqn. 1 has been modified [4] by replacing all difference terms involving $x_1$, *e.g.* $(x_1 - x_2)$, by $(2x_1 - 1)$. Thus, when the modified form of eqn. 1 is applied to ternary mixtures only two terms, namely $(x_1^1 - x_2^1)$ and $(x_1^1 - x_3^1)$, will need to be replaced by $(2x_1^1 - 1)$. For the quaternary mixture three terms will be replaced, and for quinary mixtures the four terms involving $x_1^1$ will be replaced by $(2x_1^1 - 1)$. This modification (which will be referred to as eqn. 2) was originally intended for mixtures containing one polar component, or for mixtures where one of the components was appreciably different in some manner from the others.

A combination of eqns. 1 and 2 enables the following equation to be obtained for ternary mixtures :

$$\begin{aligned}\Delta H_{123} = {} & x_1^1 x_2^1[H_{12}^{\circ} + H_{12}^1(x_1^1 - x_2^1 - x_3^1/2) + H_{12}^{11}(x_1^1 - x_2^1 - x_3^1/2)^2 + \ldots] \\ & + x_1^1 x_3^1[H_{13}^{\circ} + H_{13}^1(x_1^1 - x_3^1 - x_2^1/2) + H_{13}^{11}(x_1^1 - x_3^1 - x_2^1/2)^2 + \ldots] \\ & + x_2^1 x_3^1[H_{23}^{\circ} + H_{23}^1(x_2^1 - x_3^1) + H_{23}^{11}(x_2^1 - x_3^1)^2 + \ldots] \quad . \quad (4)\end{aligned}$$

*i.e.* difference terms involving $x_1^1$, *e.g.* $(x_1^1 - x_2^1)$, are replaced by $(x_1^1 - x_2^1 - x_3^1/2)$. For quaternary and quinary mixtures the replacement terms for $(x_1^1 - x_2^1)$ will be :

$[x_1^1 - x_2^1 - (x_3^1 + x_4^1)/2]$ and $[x_1^1 - x_2^1 - (x_3^1 + x_4^1 + x_5^1)/2]$, respectively.

This equation will be referred to as eqn. 4.

[1] Part II, Mathieson and Thynne, preceding paper.
[3] Redlich and Kister, *Ind. Eng. Chem.*, 1948, **40**, 31.
[4] Scatchard, Goates, Ticknor, and Macastney, *J. Amer. Chem. Soc.*, 1952, **74**, 3724.

Tsao and Smith [5] proposed an equation for the prediction of the heats of mixing of ternary systems which may be stated :

$$\Delta H_{123} = H_{12}[x_2^1/(x_2^1 + x_3^1)] + H_{13}[x_3^1/(x_2^1 + x_3^1)] + H_{23}(1 - x_1^1) \quad . \quad (3)$$

where, as before :

$$H_{12} = x_1x_2[H_{12}^\circ + H_{12}^1(x_1 - x_2) + H_{12}^{11}(x_1 - x_2)^2 + \ldots] \text{ etc.}$$

The values of the heats of mixing calculated from eqns. 1—4 are shown together with the experimental values in Tables 1—9. When eqn. 1 was applied to the 73 results obtained for the ternary systems (*i.e.* including 31 results given in Part I) then an average deviation

TABLE 1. *Benzene–cyclohexane–hexane.*

| | | | $\Delta H_m$ | | | | |
|---|---|---|---|---|---|---|---|
| $x_1$ | $x_2$ | $x_3$ | Exptl. | Eqn. 1 | Eqn. 2 | Eqn. 3 | Eqn. 4 |
| 0·266 | 0·398 | 0·335 | 745 | 761 | 699 | 950 | 695 |
| 0·383 | 0·335 | 0·282 | 874 | 895 | 841 | 996 | 866 |
| 0·307 | 0·376 | 0·317 | 803 | 820 | 757 | 983 | 787 |
| 0·344 | 0·356 | 0·300 | 841 | 854 | 799 | 996 | 828 |
| 0·424 | 0·282 | 0·294 | 866 | 920 | 870 | 979 | 895 |
| 0·455 | 0·230 | 0·315 | 870 | 912 | 870 | 937 | 895 |
| 0·578 | 0·250 | 0·172 | 883 | 912 | 887 | 799 | 895 |
| 0·359 | 0·479 | 0·162 | 816 | 841 | 795 | 912 | 812 |
| 0·309 | 0·517 | 0·174 | 757 | 782 | 732 | 887 | 749 |
| 0·295 | 0·527 | 0·178 | 741 | 761 | 711 | 874 | 732 |
| 0·300 | 0·578 | 0·122 | 749 | 741 | 695 | 803 | 711 |

TABLE 2. *Benzene–toluene–heptane.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 0·166 | 0·733 | 0·101 | 293 | 268 | 284 | 406 | 280 |
| 0·161 | 0·741 | 0·098 | 284 | 255 | 272 | 397 | 268 |
| 0·144 | 0·768 | 0·088 | 255 | 234 | 243 | 351 | 247 |
| 0·308 | 0·400 | 0·292 | 640 | 640 | 682 | 766 | 644 |
| 0·437 | 0·298 | 0·265 | 695 | 678 | 715 | 833 | 686 |
| 0·673 | 0·232 | 0·095 | 393 | 377 | 393 | 540 | 368 |
| 0·320 | 0·458 | 0·222 | 552 | 548 | 586 | 506 | 573 |

TABLE 3. *Benzene–toluene–hexane.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 0·073 | 0·716 | 0·211 | 222 | 192 | 205 | 351 | 201 |
| 0·073 | 0·715 | 0·212 | 222 | 192 | 205 | 351 | 201 |
| 0·084 | 0·675 | 0·241 | 238 | 217 | 234 | 414 | 230 |
| 0·079 | 0·693 | 0·228 | 238 | 209 | 222 | 385 | 217 |
| 0·078 | 0·698 | 0·224 | 251 | 209 | 222 | 385 | 217 |
| 0·182 | 0·294 | 0·524 | 519 | 494 | 523 | 686 | 498 |
| 0·204 | 0·209 | 0·587 | 602 | 565 | 590 | 711 | 556 |

TABLE 4. *Toluene–cyclohexane–heptane.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 0·157 | 0·767 | 0·076 | 402 | 364 | 364 | 435 | 368 |
| 0·183 | 0·401 | 0·416 | 510 | 527 | 531 | 628 | 527 |
| 0·404 | 0·398 | 0·198 | 623 | 653 | 657 | 858 | 657 |
| 0·480 | 0·271 | 0·249 | 703 | 661 | 669 | 849 | 669 |
| 0·647 | 0·235 | 0·118 | 531 | 577 | 577 | 711 | 577 |
| 0·649 | 0·198 | 0·153 | 548 | 573 | 577 | 707 | 573 |

TABLE 5. *Toluene–cyclohexane–hexane.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 0·360 | 0·450 | 0·190 | 615 | 586 | 590 | 753 | 586 |
| 0·384 | 0·434 | 0·182 | 602 | 594 | 598 | 753 | 598 |
| 0·722 | 0·195 | 0·083 | 481 | 464 | 469 | 577 | 469 |
| 0·749 | 0·177 | 0·074 | 435 | 435 | 439 | 536 | 439 |
| 0·785 | 0·150 | 0·065 | 393 | 389 | 389 | 473 | 389 |

TABLE 6. *Benzene–toluene–cyclohexane.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 0·174 | 0·255 | 0·571 | 602 | 640 | 678 | 527 | 661 |
| 0·261 | 0·239 | 0·500 | 669 | 707 | 741 | 636 | 749 |
| 0·338 | 0·245 | 0·417 | 741 | 728 | 749 | 736 | 741 |
| 0·386 | 0·296 | 0·318 | 678 | 661 | 669 | 782 | 669 |
| 0·462 | 0·284 | 0·254 | 602 | 611 | 611 | 761 | 615 |
| 0·562 | 0·239 | 0·198 | 536 | 519 | 510 | 686 | 515 |

[5] Tsao and Smith, "Applied Thermodynamics," *Chem. Eng. Progr. Symp. Series* No. 7, 1953, **49**, 107.

TABLE 7. *Toluene–cyclohexane–heptane–hexane.*

| | | | | $\Delta H_m$ | | | |
|---|---|---|---|---|---|---|---|
| $x_1$ | $x_2$ | $x_3$ | $x_4$ | Exptl. | Eqn. 1 | Eqn. 2 | Eqn. 4 |
| 0·170 | 0·383 | 0·124 | 0·323 | 473 | 464 | 464 | 464 |
| 0·456 | 0·166 | 0·266 | 0·112 | 565 | 611 | 607 | 611 |
| 0·188 | 0·423 | 0·137 | 0·243 | 510 | 498 | 494 | 494 |
| 0·166 | 0·347 | 0·121 | 0·366 | 427 | 448 | 448 | 448 |
| 0·180 | 0·178 | 0·300 | 0·342 | 389 | 423 | 427 | 423 |
| 0·225 | 0·147 | 0·255 | 0·373 | 435 | 444 | 452 | 448 |
| 0·207 | 0·136 | 0·200 | 0·458 | 410 | 418 | 423 | 418 |
| 0·216 | 0·142 | 0·300 | 0·342 | 410 | 440 | 448 | 444 |

TABLE 8. *Benzene–cyclohexane–heptane–hexane.*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 0·360 | 0·148 | 0·220 | 0·272 | 833 | 912 | 849 | 883 |
| 0·275 | 0·302 | 0·167 | 0·256 | 782 | 829 | 766 | 782 |
| 0·342 | 0·211 | 0·208 | 0·239 | 874 | 912 | 829 | 874 |
| 0·194 | 0·319 | 0·235 | 0·252 | 636 | 699 | 619 | 657 |
| 0·375 | 0·231 | 0·171 | 0·223 | 920 | 946 | 879 | 904 |
| 0·289 | 0·269 | 0·199 | 0·243 | 816 | 854 | 766 | 808 |
| 0·312 | 0·226 | 0·189 | 0·273 | 879 | 912 | 858 | 879 |
| 0·193 | 0·318 | 0·221 | 0·268 | 657 | 695 | 615 | 657 |
| 0·500 | 0·137 | 0·247 | 0·116 | 987 | 1000 | 941 | 979 |
| 0·364 | 0·225 | 0·222 | 0·189 | 891 | 946 | 862 | 904 |
| 0·185 | 0·153 | 0·309 | 0·353 | 602 | 623 | 556 | 598 |
| 0·157 | 0·129 | 0·430 | 0·284 | 531 | 548 | 490 | 535 |
| 0·492 | 0·190 | 0·239 | 0·080 | 954 | 1017 | 962 | 996 |
| 0·198 | 0·421 | 0·311 | 0·069 | 686 | 720 | 640 | 678 |
| 0·212 | 0·479 | 0·236 | 0·073 | 715 | 724 | 644 | 678 |

TABLE 9. *Benzene–toluene–cyclohexane–hexane–heptane.*

| | | | | | $\Delta H_m$ | | | |
|---|---|---|---|---|---|---|---|---|
| $x_1$ | $x_2$ | $x_3$ | $x_4$ | $x_5$ | Exptl. | Eqn. 1 | Eqn. 2 | Eqn. 4 |
| 0·290 | 0·198 | 0·238 | 0·099 | 0·175 | 812 | 845 | 836 | 849 |
| 0·192 | 0·172 | 0·216 | 0·086 | 0·234 | 766 | 791 | 795 | 799 |
| 0·235 | 0·174 | 0·290 | 0·087 | 0·214 | 766 | 828 | 828 | 828 |
| 0·335 | 0·204 | 0·207 | 0·101 | 0·153 | 816 | 845 | 833 | 841 |
| 0·156 | 0·152 | 0·449 | 0·101 | 0·142 | 674 | 711 | 732 | 728 |
| 0·255 | 0·154 | 0·370 | 0·104 | 0·116 | 766 | 816 | 828 | 828 |
| 0·267 | 0·278 | 0·175 | 0·118 | 0·162 | 732 | 787 | 770 | 787 |
| 0·208 | 0·208 | 0·284 | 0·240 | 0·060 | 745 | 766 | 766 | 770 |
| 0·293 | 0·158 | 0·337 | 0·105 | 0·107 | 782 | 841 | 849 | 849 |
| 0·299 | 0·165 | 0·246 | 0·109 | 0·181 | 833 | 862 | 849 | 862 |
| 0·291 | 0·207 | 0·240 | 0·202 | 0·060 | 812 | 812 | 804 | 812 |
| 0·183 | 0·151 | 0·302 | 0·254 | 0·110 | 724 | 745 | 741 | 749 |
| 0·230 | 0·143 | 0·284 | 0·239 | 0·104 | 791 | 791 | 778 | 791 |
| 0·258 | 0·287 | 0·178 | 0·120 | 0·157 | 766 | 782 | 766 | 782 |
| 0·347 | 0·145 | 0·198 | 0·100 | 0·210 | 820 | 891 | 874 | 883 |
| 0·293 | 0·245 | 0·189 | 0·095 | 0·178 | 770 | 820 | 803 | 816 |
| 0·330 | 0·184 | 0·170 | 0·115 | 0·201 | 791 | 858 | 836 | 836 |
| 0·308 | 0·193 | 0·207 | 0·105 | 0·187 | 782 | 853 | 836 | 849 |

of the predicted heat of mixing from the measured heat of +0·9% was observed. The average deviation given by eqn. 2 was −0·8%, and by eqn. 4 less than +0·1%. These deviations lie well within the range of experimental error. Eqn. 3 gives a much poorer representation of the results, the average deviation being +8·1%.

Application of eqns. 1, 2, and 4 to the quaternary mixtures resulted in average deviations of +4·5, −1·6, and +1·5%, respectively. Since the experimental error is about ±5% for such mixtures, these deviations are satisfactory.

The average deviations for the quinary mixture were, for equations 1, 2, and 4, +5·0, +4·2, and +5·1%, respectively. These values are rather high, but again in view of the possible experimental error, are reasonable.

From a consideration of these results, it seems that for hydrocarbon systems the heats of mixing of multicomponent systems may be predicted with considerable accuracy, when the heats of mixing of the constituent binary mixtures are known.

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THE UNIVERSITY, NOTTINGHAM. [*Received, May 2nd,* 1956.]

## 722. *Studies in Relation to Biosynthesis. Part VIII.* The Structure of Mycelianamide.*

By A. J. Birch, R. A. Massy-Westropp, and R. W. Rickards.

Mycelianamide, $C_{22}H_{28}O_5N_2$, gives by the action of ammonia *p*-myceloxybenzamide which is very similar to, but not identical with *p*-geranyloxybenzamide. Hydrogenation produces deoxymycelianamide, $C_{22}H_{28}O_3N_2$, which is hydrolysed by acid to *p*-hydroxyphenylpyruvic acid and alanine. Reduction with sodium and liquid ammonia gives methylgeraniolene. Ozonolysis gives acetaldehyde and acetone. On the basis of this and previously published evidence, together with considerations based on the general properties of the substance, the formula

[VIII; R = $CMe_2$:$CH{\cdot}CH_2{\cdot}CH_2{\cdot}C(:CHMe){\cdot}CH_2{\cdot}$]

is suggested.

Mycelianamide, $C_{22}H_{28}O_5N_2$, from the mycelium of strains of *Penicillium griseofulvum* Dierckx was examined by Oxford and Raistrick,[1] who suggested the structural formula (I). They showed that ammonia gave *p*-myceloxybenzamide (II; R = $NH_2$) and mild alkaline hydrolysis gave *p*-myceloxybenzoic acid (II; R = OH). Acid hydrolysis gave ammonia and substance (III), together with an unsaturated hydrocarbon, $C_{10}H_{16}$, "mycelene," which contained a persistent oxygenated impurity. Mycelene, examined by Simonsen (quoted by Oxford and Raistrick [1]), appeared to be a monocyclic hydrocarbon, and ozonolysis gave formaldehyde and a diketone, $C_8H_{14}O_2$. It was suggested that the mycelyl radical is derived from an allyl alcohol because of the ease of fission of the ether link.

Mycelianamide gives a red ferric test, is soluble in carbonate solutions, and is non-basic. Oxford and Raistrick, therefore, suggested the partial formula (I), the asymmetric centre being marked by an asterisk.

We have shown that this formula is incorrect since the substance is recovered with unchanged optical rotation after dissolution in sodium carbonate solution. The enolic salt derived from (I) in such a reaction would be inactive.

The problem of the structure of mycelianamide resolves itself into two parts: determination of the structure of the nitrogen-containing portion of the molecule, and determination of the structure of the mycelyl radical.

*The Nucleus.*—*C*-Methyl analyses of mycelianamide probably indicate three such groups; myceloxybenzamide appears to contain two *C*-methyl groups; consequently the nitrogen-containing portion of the molecule must contain one. This portion confers the solubility in carbonate solutions and the positive ferric test. The formation of ammonia, carbon dioxide, and compound (III) on acid hydrolysis, and of (II; R = $NH_2$ or OH) under alkaline conditions suggests an acyldioxopiperazine, as type (VII) where the position of the hydroxyl group cannot be defined with certainty. Support for this was obtained by detection of alanine among the products of acid hydrolysis. However, mild reduction with zinc dust and acetic acid produced in good yield deoxymycelianamide, $C_{22}H_{28}O_3N_2$, lacking two oxygen atoms; this is insoluble in alkali, gives no ferric test, and has an ultraviolet absorption very similar to that of mycelianamide itself. There is only slight alteration in the chromophore on reduction (from $\lambda_{max.}$ 231, 321 mμ to $\lambda_{max.}$ 225, 317 mμ) the absorption being similar to that of *p*-methoxybenzylideneacetone ($\lambda_{max.}$ 232, 317 mμ). The slight shift to shorter wavelengths on reduction would be expected on removal of hydroxyl groups from nitrogen. Deoxymycelianamide has a strong band at 1675 cm.$^{-1}$ which is characteristic of unstrained cyclic amides, including dioxopiperazines. This suggests that mycelianamide is a cyclic bisacylhydroxylamine, a probable formula being (VIII; R = $C_{10}H_{17}$). Support for this assumption was obtained by examining the hydrolysis of deoxymycelianamide, which produced alanine and *p*-hydroxyphenylpyruvic acid. In order to explain the products of hydrolysis of mycelianamide itself the formation

* Part VII—Birch, Massy-Westropp and Moye, *Austral. J. Chem.*, 1955, **8**, 539.

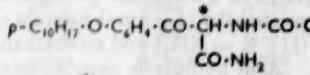
[1] Oxford and Raistrick, *Biochem. J.*, 1948, **42**, 323.

of an intermediate acyldioxopiperazine would appear to be necessary. The formula originally assigned to mycelianamide itself [2] is therefore rather that of such an intermediate. Formation of this would involve an internal rearrangement for which, so far as we are aware, no analogies exist although it has affinities with the rearrangement of 2-methylpyridine 1-oxides to 2-hydroxymethylpyridine derivatives.

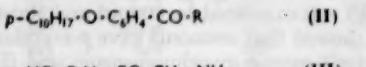
A number of mould products are known which contain the acylhydroxylamine, or related groups, including mycobactin, cycloserine (oxamycin), nocardamin, and aspergillin.

*The Side-chain.*—The $C_{10}$-formula of the mycelyl radical suggests the presence of a terpenoid side-chain, which we particularly desire in a mould metabolic product for biosynthetic studies.

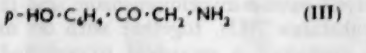
The presence of a geranyl side-chain as in (IX) is not incompatible with Simonsen's results, since geraniol is known to undergo cyclisation under the conditions used in the hydrolysis. Among the products of this cyclisation are dipentene (IV), which could give formaldehyde on ozonolysis, and α-terpinene (V) which could give a diketone $C_8H_{14}O_2$



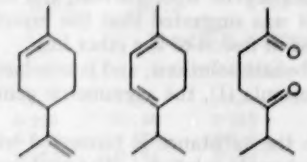
(I)



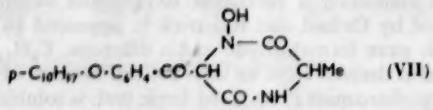
(II)



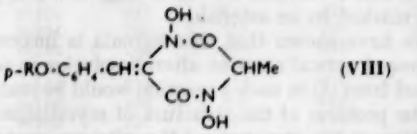
(III)



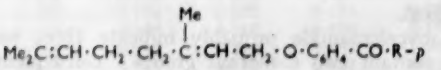
(IV) (V) (VI)



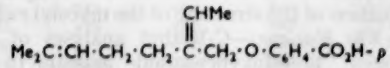
(VII)



(VIII)



(IX)



(X)

(VI). The persistent oxygenated impurity could well be a tertiary alcohol like α-terpineol. Ozonolysis of mycelianamide gave rise chiefly to acetone and some acetaldehyde, and it was originally believed that the latter was derived from the alanine residue. The mycelyl radical would on the basis of these properties and its optical inactivity probably be identical with the geranyl radical.[2] Accordingly *p*-geranyloxybenzoic acid (IX; R = OH) and *p*-geranyloxybenzamide (IX; R = $NH_2$) were synthesised for comparison with the corresponding mycelyl compounds.

Lauer and Labriola [3] record m. p. 113—114° for *p*-geranyloxybenzoic acid, compared with m. p. 118—120° for *p*-myceloxybenzoic acid. The action of geranyl bromide on methyl *p*-hydroxybenzoate in the presence of potassium carbonate, and hydrolysis, gave several fractions of acid, m. p. 117—118° and m. p. 119—120°, which could not be appreciably altered by recrystallisation. Both fractions were undepressed in m. p. by *p*-myceloxybenzoic acid. Some difficulty was experienced in preparing pure *p*-geranyloxybenzamide. The acid chloride, prepared by the action of thionyl chloride, reacted with ammonia to give specimens melting between 105° and 114°, which could not be purified further by crystallisation. However, phosphorus tribromide and pyridine, followed by

[2] Birch, Massy-Westropp, and Rickards, *Chem. and Ind.*, 1955, 1599.
[3] Lauer and Labriola, *J. Amer. Chem. Soc.*, 67, 1254.

ammonia, gave an amide, m. p. 117—119° undepressed by *p*-myceloxybenzamide, m. p. 119—120·5°. It was originally considered [2] that this evidence proved the identity of the radicals. However, we were later able to measure the infrared spectra, and although the resemblances between the spectra of the synthetic substances and of the hydrolysis products are great there exist some slight differences in positions and intensities of bands in the region 8—14 μ which are greater than would be expected if the substances are in fact identical. We have accordingly examined the ozonolysis of *p*-myceloxybenzamide. From this reaction were obtained acetone and acetaldehyde, and none of the expected lævulaldehyde or acid. Control experiments ensured that the acetaldehyde could not be derived from the solvents used. Reduction of mycelianamide with sodium and methanol in liquid ammonia should remove the side-chain by hydrogenolysis to give a hydrocarbon [4] probably identical with methylgeraniolene (2 : 6-dimethylocta-2 : 6-diene). Reduction gave an oil which, from its infrared spectrum, appears to be identical with this hydrocarbon obtained by similar reduction of linalool. Some minor differences in the spectra may be due to *cis-trans* isomerism, but the crystalline tetrabromide, m. p. 88—89°, was undepressed in m. p. by an authentic specimen, and had an identical infrared spectrum. We therefore suggest (X) as the most probable formula for *p*-myceloxybenzoic acid, this formulation being supported by the close resemblance to *p*-geranyloxybenzoic acid and by the general properties of the mycelyl radical including its ready removal by dilute acid and its optical inactivity. Mycelianamide is, therefore, probably [VIII; R = $CMe_2$:$CH{\cdot}CH_2{\cdot}CH_2{\cdot}C(:CHMe){\cdot}CH_2{\cdot}$]. Further work is in progress.

Biochemical studies with isotopically labelled acetic acid and labelled tyrosine show that both of these substances are readily incorporated by the mould into the mycelianamide molecule.[5] The results of degradations of these labelled compounds will be reported.

## Experimental

M. p.s are uncorrected.

Mycelianamide was obtained from the mycelium of *Penicillium griseofulvum* Dierckx (Raistrick's strain P.68) by Oxford and Raistrick's method; it had m. p. 171° (Found: *C*-Me, 10·3. Calc. for $C_{22}H_{33}O_5N_3$: 3*C*-Me, 11·25%).

*p*-Myceloxybenzamide, m. p. 119—120·5°, was obtained as described [1] (Found: *C*-Me, 7·9. Calc. for $C_{17}H_{23}O_3N$: 2*C*-Me, 11·0%). Hydrolysis with refluxing saturated methanolic potassium hydroxide for 3·5 hr. gave *p*-myceloxybenzoic acid, m. p. 117—119° after crystallisation from light petroleum (b. p. 60—80°).

p-*Geranyloxybenzoic Acid.*—The preparation was essentially as described by Lauer and Labriola,[3] with methyl instead of ethyl *p*-hydroxybenzoate. After hydrolysis of the ester by refluxing in methanolic potassium hydroxide (8%) for 1·5 hr., and acidification with hydrochloric acid the oily precipitate was only partly soluble in hot benzene. The insoluble portion (undecomposed sodium salt) on treatment with acetic acid gave *p*-geranyloxybenzoic acid, m. p. 119—120° (Found: C, 74·2; H, 8·1. Calc. for $C_{17}H_{22}O_3$: C, 74·4; H, 8·1%). The benzene solution on similar treatment gave a less pure material, the m. p. of which was raised to 117—118° by repeated crystallisation from light petroleum (b. p. 60—80°). Both fractions, which had almost identical infrared spectra, were undepressed in m. p. on admixture with *p*-myceloxybenzoic acid, m. p. 117—119°.

p-*Geranyloxybenzamide.*—*p*-Geranyloxybenzoic acid (200 mg.) in pyridine (0·5 c.c.) was treated slowly at 0° with phosphorus tribromide (100 mg.) and left for 30 min. at room temperature. Concentrated aqueous ammonia was then added and the mixture extracted with benzene. Several crystallisations from benzene–light petroleum (b. p. 40—60°) yielded p-*geranyloxybenzamide* (50 mg.), m. p. 117—119° (Found: C, 74·3; H, 8·5. $C_{17}H_{23}O_2N$ requires C, 74·7; H, 8·5%). Its m. p. was undepressed by *p*-myceloxybenzamide, m. p. 119—120·5°.

*Ozonolysis of Mycelianamide.*—Mycelianamide (1 g.) in glacial acetic acid (purified by refluxing with chromic oxide) was ozonised at 20° until ozone emerged freely, zinc dust and a little water were added, and the mixture was slowly distilled into 2 : 4-dinitrophenylhydrazine

[4] Birch, *J.*, 1945, 809.
[5] Birch, Massy-Westropp, and Moye, unpublished work.

in 2N-hydrochloric acid. The resulting mixture was chromatographed on alumina in ethyl acetate–light petroleum (b. p. 60—80°), and arbitrary fractions collected. After several crystallisations from ethanol fractions of m. p. 124° and m. p. 160° were obtained, undepressed by authentic specimens of the derivatives of acetone (m. p. 126°) and acetaldehyde (m. p. 166°), respectively. Paper chromatography with heptane–methanol also confirmed these identifications: $R_F$ (acetone derivative) 0·54; $R_F$ (acetaldehyde derivative) 0·37. A blank test on the solvent gave neither of these derivatives.

*Ozonolysis of* p-*Myceloxybenzamide.*—*p*-Myceloxybenzamide (40 mg.) in glacial acetic acid was ozonised as above, and paper chromatography of the 2-4-dinitrophenylhydrazone in heptane–methanol showed the presence of acetone and acetaldehyde derivatives ($R_F$ 0·54 and 0·37).

*Acid Hydrolysis of Mycelianamide.*—Mycelianamide (0·5 g.) was refluxed under nitrogen for 6 hr. with hydrochloric acid (0·5N., 80 c.c.) with slow distillation to remove mycelene. The residue was extracted with ether several times and the aqueous solution evaporated to dryness under reduced pressure at a low temperature. The solid residue was submitted to paper chromatography,[6] phenol saturated with water and containing ammonia (3%) being used. The $R_F$ values of natural alanine and this material were the same: 0·62. Similarly, *iso*butyric acid saturated with water being used, an $R_F$ of 0·35 was obtained for both alanine and the hydrolysis product.

*Deoxymycelianamide.*—Zinc dust (2 g.) was added gradually during 15 hr. with occasional shaking and warming to mycelianamide (0·5 g.) in glacial acetic acid (30 c.c.). After a further 2 days the mixture was warmed and filtered, the zinc residues being extracted three times with boiling ethanol (*ca.* 10 c.c.). The combined solutions were evaporated to dryness under reduced pressure and the residue washed several times with water and crystallised from ethanol. The deoxymycelianamide (280 mg.) was obtained as colourless needles, m. p. 170°, $[\alpha]_D$ −5° ($CHCl_3$) (Found: C, 71·5; H, 7·6. $C_{23}H_{24}O_3N_2$ requires C, 71·7; H, 7·7%). It was insoluble in sodium carbonate solution and gave no ferric test. The ultraviolet absorption in ethanol: $\lambda_{max.}$ 225 mμ (ε 14,000), 317 mμ (ε 2200), resembles that of mycelianamide: $\lambda_{max.}$ 231 mμ (ε 11,000), 321 mμ (ε 23,000).

*Acid Hydrolysis of Deoxymycelianamide.*—Deoxymycelianamide (50 mg.) was refluxed with N-hydrochloric acid in an atmosphere of nitrogen for 7 hr. A negligible amount of carbon dioxide was evolved. After filtration the solution was treated with 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid, and the derivative extracted with ether and removed therefrom with sodium hydrogen carbonate solution. Crystallisation from aqueous acetic acid gave yellow needles, m. p. 171° undepressed by *p*-hydroxyphenylpyruvic acid 2 : 4-dinitrophenylhydrazone, m. p. 172°. Paper chromatography with butanol : ethanol : water (4 : 1 : 4) [7] confirmed the identification, giving $R_F$ 0·75 for the authentic substance and that obtained above. The infrared spectra were also identical, with the following bands: 3470 m, 3390 m, 3170 w, 3070 w, 1680 w, 1615 s, 1570 m, 1520 s, 1420 m, 1340 s, 1310 s, 1270 m, 1215 m, 1135 m, 1110 s, 1090 m, 930 w, 860 w, 840 w, 800 w cm.$^{-1}$.

The original hydrolysis solution on evaporation and paper chromatography with phenol–water (see above) was shown to contain alanine, $R_F$ 0·52.

*Reduction of Mycelianamide.*—Mycelianamide (3 g.) in warm methanol (30 c.c.) was added to liquid ammonia (200 c.c.), followed by sodium (6 g.) in small pieces. The initial precipitate rapidly dissolved. After addition of water (100 c.c.) small droplets of oil could be observed. These were collected by the addition of very small quantities of ether. The solution was well washed with water and evaporated finally at 100° for some time leaving an oil with a characteristic odour. Distillation (bath temp. 190°) gave an oil (0·57 g.). The infrared spectrum showed the following bands: 2900 s, 2710 w, 1840 w, 1670 m, 1640 w, 1460 s, 1387 s, 1350 m, 1332 w, 1310 w, 1265 w, 1215 m, 1200 w, 1157 m, 1112 s, 1098 m, 1150 m, 1135 m, 990 m, 960 w, 912 m, 882 w, 827 s, 790 m, 777 m, 740 m cm.$^{-1}$ (liquid film).

Authentic methylgeraniolene from linalool [8] showed the following bands: 2900 s, 2700 w, 1830 w, 1667 m, 1635 w, 1450 s, 1380 s, 1350 m, 1330 w, 1312 w, 1210 m, 1200 w, 1155 m, 1112 s, 1095 m, 1055 w, 1035 w, 987 m, 965 w, 912 w, 885 s, 790 m, 775 m, 740 w cm.$^{-1}$.

The tetrabromide of the substance from mycelianamide was prepared by the method of Schimmel and Co.[8] and had m. p. 88—89°, undepressed by the derivative similarly prepared from authentic methylgeraniolene. The infrared spectra (C in $CS_2$) were identical, with the

[6] Consden, Gordon, and Martin, *Biochem. J.*, 1944, **38**, 224.
[7] Cavallini, Frontali, and Toshi, *Nature*, 1949, **163**, 568.
[8] Schimmel and Co., *Chem. Centr.*, 1912, **33**, 245.

following bands: **2942 s, 2900 s, 1380 s, 1370 s, 1330 w, 1280 m, 1240 s, 1210 s, 1160 m, 1140 m, 1100 s, 1060 s, 1020 w, 990 m, 955 m, 940 m, 915 w, 855 w, 795 s, 750 w** cm.$^{-1}$.

We are grateful to the University of Sydney for a Research Scholarship and the University of Manchester for a Science Research Scholarship (R. A. M.-W.), to Dr. P. W. Brian for a specimen of the mould, to Dr. B. J. Ralph (N.S.W. University of Technology) for assistance in growing the mould, to Messrs. Timbrol (Rhodes, N.S.W.) for some infrared spectra, and to Mr. C. J. Moye for the preparation of methylgeraniolene.

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## 723. *Raman Spectrum of the Tetrachlorogallate Ion* ($GaCl_4^-$) *in Aqueous Solution.*

By L. A. WOODWARD and A. A. NORD.

An approximately 1·5M-aqueous solution of gallium trichloride containing 6·3M-hydrochloric acid gives four Raman frequencies, which are attributed to the $GaCl_4^-$ ion of regular tetrahedral shape: $\nu_2$ ($E$) = **114** cm.$^{-1}$, strong, sharp, depolarised; $\nu_4$ ($F_2$) = **149** cm.$^{-1}$, strong, sharp, depolarised; $\nu_1$ ($A_1$) = **346** cm.$^{-1}$, very strong, sharp, highly polarised; and $\nu_3$ ($F_2$) = **386** cm.$^{-1}$, weak, diffuse, depolarised.

IN a previous paper [1] we described the Raman spectrum of the tetrabromogallate ion, $GaBr_4^-$, in an aqueous solution of gallium tribromide containing excess of hydrobromic acid. We have now investigated a solution of gallium trichloride (1·5M) containing an excess of hydrochloric acid (6·3M) and have observed an entirely analogous Raman spectrum. The observed frequency shifts, estimated intensities, appearances of lines, states of polarisation, and assignments are given in Table 1.

TABLE 1. *Raman spectrum of the* $GaCl_4^-$ *ion in aqueous solution.*

| $\Delta\nu$ (cm.$^{-1}$) | **114** | **149** | **346** | **386** |
|---|---|---|---|---|
| Intensity | Strong | Strong | Very strong | Weak |
| Appearance | Sharp | Sharp | Sharp | Diffuse |
| Polarisation | Depolarised | Depolarised | Highly polarised | Depolarised |
| Assignment | $\nu_2$ ($E$) | $\nu_4$ ($F_2$) | $\nu_1$ ($A_1$) | $\nu_3$ ($F_2$) |

As with the tetrabromogallate ion [1] the observation of four Raman frequencies, one highly polarised and the other three depolarised, provides evidence that the scattering species is of the regular tetrahedral $XY_4$ type (point group $T_d$); and the spectrum can be attributed with confidence to the tetrachlorogallate ion $GaCl_4^-$. This must be the predominant complex in the solution investigated.

This ion is isoelectronic with both $GeCl_4$ and $ZnCl_4^{2-}$. The observed vibrational frequencies are compared in Table 2, where the values for $GeCl_4$ are as given by Herzberg [2] and the values for $ZnCl_4^{2-}$ are those of Delwaulle.[3] For the latter species, only $\nu_1$ could be determined satisfactorily: $\nu_3$ was not observed, no doubt owing to its weakness, its probable diffuseness, and its proximity to the much stronger $\nu_1$, while at lower frequencies the spectrum showed only a rather wide unresolved band which doubtless includes both $\nu_2$ and $\nu_4$.

[1] Woodward and Nord, *J.*, 1955, 2655.
[2] Herzberg, "Molecular Spectra and Molecular Structure," van Nostrand Co., New York, 1945, Vol. II, p. 167.
[3] Delwaulle, *Compt. rend.*, 1955, **240**, 2132.

From Table 2 it is seen that there is a decrease of all four fundamental frequencies as we pass from the neutral $GeCl_4$ molecule to the singly negatively charged $GaCl_4^-$ ion, and that the decrease continues for $\nu_1$ (and probably also for the other fundamentals) as we pass from $GaCl_4^-$ to the doubly-negatively charged ion $ZnCl_4^{2-}$. This behaviour is quite similar to that observed for other corresponding isoelectronic sets, such as [4] $SnBr_4$, $InBr_4^-$, and $CdBr_4^{2-}$, and further supports the view that the spectrum of Table 1 is to be attributed

TABLE 2. *Fundamental vibrational frequencies (cm.$^{-1}$) of isoelectronic species.*

| | $\nu_2$ | $\nu_4$ | $\nu_1$ | $\nu_3$ |
|---|---|---|---|---|
| $GeCl_4$ | 134 | 172 | 396 | 453 |
| $GaCl_4^-$ | 114 | 149 | 346 | 386 |
| $ZnCl_4^{2-}$ | 61—82 | | 282 | ? |

to the tetrachlorogallate ion. As far as the totally symmetrical " breathing " frequencies $\nu_1$ are concerned, the progressive decrease indicates that the stretching force $k$ of the metal–chlorine bond likewise decreases in the order given. The values of $10^{-5}k$ calculated on the basis of a simple valency force field are: $GeCl_4$, 3·28; $GaCl_4^-$, 2·50; and $ZnCl_4^{2-}$, 1·64 dynes per cm. The value of $k$ (or of $\nu_1$) for the singly charged species $GaCl_4^-$ is not midway between the corresponding values for the isoelectronic neutral and doubly charged species, $GeCl_4$ and $ZnCl_4^{2-}$. In fact the decrease in passing from $GaCl_4^-$ to $ZnCl_4^{2-}$ is greater than that in passing from $GeCl_4$ to $GaCl_4^-$. This kind of non-linear variation of $k$ with the atomic number of the central atom has been noted [5] for other sets of isoelectronic species of the regular tetrahedral $XY_4$ type.

## EXPERIMENTAL

A weighed quantity of pure gallium, supplied by Messrs. Johnson, Matthey and Co., was dissolved in sufficient concentrated hydrochloric acid to give a 1·5M-solution of gallium trichloride containing approximately 6·3M-excess of acid. The metal dissolved slowly but completely, to a clear colourless solution which, however, continued to evolve hydrogen (apparently from irregularities on the surface of the glass vessel) and was strongly reducing. At this stage the solution no doubt contained gallium in a lower than tervalent state. Before use it was kept in a warm water-bath until hydrogen evolution had ceased, by which time the reducing properties had disappeared.

The Raman spectra were photographed with the apparatus previously described.[1,6] Excitation was by means of a " Toronto arc," and the principal primary line was Hg 4358 Å. Qualitative information on the states of polarisation of the Raman lines was obtained by the method of polarised incident light, suitable Polaroid cylinders surrounding the Raman tube. The $\Delta\nu$ values were measured in the usual way with a copper-arc spectrum as standard. The estimated limits of error are about $\pm 2$ cm.$^{-1}$ for strong sharp lines. The value for $\nu_3$ given in Table 1 may be less precise, as its Raman line is weak and diffuse and lies rather near the very intense line of $\nu_1$. With natural light the Raman spectrum of $GaCl_4^-$ excited by the mercury line 4358 Å could be photographed with an exposure time of 1½ hr.

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[4] Woodward and Bill, *J.*, 1955, 1699.
[5] Woodward and Roberts, *J.*, 1956, 1170.
[6] George, Rolfe, and Woodward, *Trans. Faraday Soc.*, 1953, **49**, 375.

## 724. *Raman Spectrum and Constitution of Fused Gallium Dichloride.*

By L. A. Woodward, G. Garton, and H. L. Roberts.

The Raman spectrum of fused gallium dichloride at approx. 190° c is found to consist of four frequencies: 115 cm.$^{-1}$, strong, sharp, depolarised; 153 cm.$^{-1}$, weak, diffuse, depolarised; 346 cm.$^{-1}$, very strong, sharp, highly polarised; and 380 cm.$^{-1}$, very weak, diffuse, depolarised. This spectrum is in close agreement with that found for the $GaCl_4^-$ ion in aqueous solution. In the fused state, therefore, gallium dichloride is to be formulated as gallium(I) tetrachlorogallate(III), $[Ga^+][GaCl_4^-]$. The results do not support the hypothesis that Ga–Ga bonds are involved.

All the metals of Group IIIb show the expected valency of three: for thallium the more stable valency is one. "Gallium dichloride" has the empirical formula $GaCl_2$, which appears to indicate the intermediate valency two. First reported in 1881 by de Boisbaudran,[1] it has been comparatively little investigated and its structure has not so far been determined. If it involved bivalent gallium, the compound would be paramagnetic on account of the single unpaired electron of the gallium atom. In 1932, however, Klemm and Tilk [2] observed that solid gallium dichloride is diamagnetic, from which they concluded that the molecule must involve a covalent link between two gallium atoms, *viz.*, $Cl_2Ga–GaCl_2$.

An alternative formulation is possible, however. The compound can be written as gallium(I) tetrachlorogallate(III), $[Ga^+][GaCl_4^-]$, in which the apparent valency of two is due to univalency of one and tervalency of the other gallium atom.

The Raman effect offers a powerful method of deciding between alternative proposed molecular models of different symmetries, since these must have different rules of selection and polarisation. The position is especially favourable when, as here, one of the formulations involves only an ion for which the Raman spectrum has already been observed in other circumstances. The preceding paper [3] has described the spectrum of the tetrachlorogallate ion $GaCl_4^-$ in an aqueous solution of gallium trichloride (1·5M) containing excess of hydrochloric acid (6·3M).

*Results and Discussion.*—We have obtained the Raman spectrum of gallium dichloride in the fused state at approx. 190° c, *i.e.*, about 25° above its melting point. The annexed Table shows the observed Raman frequencies, estimated intensities, appearances of lines, and states of polarisation. The agreement with Table 1 of the preceding paper for the

*Raman spectrum of fused gallium dichloride.*

| $\Delta\nu$ (cm.$^{-1}$) | 115 | 153 | 346 | 380 |
|---|---|---|---|---|
| Intensity | Strong | Weak | Very strong | Very weak |
| Appearance | Sharp | Diffuse | Sharp | Diffuse |
| Polarisation | Depolarised | Depolarised | Highly polarised | Depolarised |

tetrachlorogallate ion is very close, and there can be little doubt that the spectrum observed for fused gallium dichloride is due to the presence of $GaCl_4^-$ ions. All the differences between corresponding $\Delta\nu$ values are probably within the limits of experimental error. In the present work these were about $\pm 3$ cm.$^{-1}$ for strong sharp lines: weaker and more diffuse lines, like those with Raman frequencies 153 and 380 cm.$^{-1}$, were subject to larger errors.

It is remarkable that the most intense and sharpest line, corresponding to the totally symmetrical "breathing" mode of the regular tetrahedral ion, should give exactly the same frequency ($\nu_1$) in the molten gallium dichloride as in the aqueous 1·5M-gallium trichloride containing excess of hydrochloric acid (6·3M), for in view of the markedly different

[1] de Boisbaudran, *Compt. rend.*, 1881, **93**, 294.
[2] Klemm and Tilk, *Z. anorg. Chem.*, 1932, **207**, 175.
[3] Woodward and Nord, preceding paper.

environments in the two cases some frequency displacement might have been expected. In this connexion the results for the isoelectronic ion $ZnCl_4^{2-}$ are of interest. The value of $\nu_1$ in aqueous solution, as observed by Delwaulle,[4] is 282 cm.$^{-1}$, while for a fused mixture of zinc chloride and potassium chloride Bues [5] found practically the same value (280 cm.$^{-1}$). For these ions, therefore, it appears that the frequency of the totally symmetrical mode is insensitive to changes of molecular environment. The lowest frequency ($\nu_2$) is also very little different in the two Tables.

On the other hand the two modes of class $F_2$ (triply degenerate) appear more weakly and more diffusely for the fused dichloride than for the $GaCl_4^-$ ion in aqueous solution. It is probable that ionic interactions in the fused state relieve the degeneracy and so affect the appearance and apparent relative intensity of these lines.

Our finding that the fused dichloride contains $GaCl_4^-$ ions is in harmony with Hampe's observation [6] that the fused salt is a conductor of electricity. If the compound involved Ga–Ga links, as suggested by Klemm and Tilk,[2] its electrical conductivity would imply that the $Cl_2Ga–GaCl_2$ molecules are at least partially dissociated into ions. The following considerations show that none of the species so formed would give a Raman spectrum consistent with the one observed.

On account of chlorine–chlorine repulsions the neutral $Cl_2Ga–GaCl_2$ molecule would probably have the staggered configuration (as in the allene molecule) with the planes of the two $GaCl_2$ groups mutually perpendicular. The point group would be $D_{2v}$, the number of Raman lines (*i.e.*, Raman-active fundamentals) would be nine, and the number polarised would be three. For the less likely planar configuration (as in the ethylene molecule, point group $D_{2h}$) the corresponding numbers would be six and three. The first stage of ionisation would give the ion $(Cl_2Ga–GaCl)^+$, which would doubtless be planar and Y-shaped (point group $C_{2v}$). For this the number of Raman lines would be nine, and the number polarised would be four. The second stage of ionisation could occur in two ways, giving either $(ClGa–GaCl)^{2+}$ or $(Cl_2Ga–Ga)^{2+}$. The former would be linear (point group $D_{\infty h}$) with three Raman lines, two of them polarised: the latter would be planar Y-shaped (point group $C_{2v}$) with six lines, three of them polarised. Further ionisation would produce the linear $(ClGa–Ga)^{3+}$, which would give three Raman lines, two polarised; and finally $(Ga–Ga)^{4+}$, which would give only one.

The observed spectrum (Table) is not consistent with the theoretical prediction either for the $Cl_2Ga–GaCl_2$ molecules or for any of the ions derivable from it. Since weak lines may sometimes escape observation, however, the argument from numbers is not always convincing. It is therefore important to note (i) that all the species here under consideration (with the obvious exception of $Ga_2^{4+}$) must have at least one totally symmetrical mode of vibration involving principally Ga–Cl stretching, and in addition one totally symmetrical mode involving principally Ga–Ga stretching; and (ii) that both of these will be expected, like all totally symmetrical stretching modes, to appear strongly in the observed Raman spectrum. It is true that the postulated Ga–Ga bond is an unusual one; but a close parallel is found in the mercurous ion $(Hg–Hg)^{2+}$ for which a strong Raman line has been observed.[7] It follows that the Raman spectrum of all the species being considered would show at least two lines that would be strong and polarised. In fact (see Table) only one polarised line is observed. The evidence therefore gives no support to the hypothesis of the Ga–Ga bond.

No sign was found of any dissociation of the tetrachlorogallate ion according to the equation $GaCl_4^- \rightleftharpoons GaCl_3 + Cl^-$, despite the absence of an excess of chlorine ions. Such a dissociation would have been followed by the formation of $Ga_2Cl_6$ molecules, and had it occurred to any appreciable extent the melt would have given the Raman frequencies characteristic of fused gallium trichloride, the most intense of which have been found [8] to be 96 and 410 cm.$^{-1}$. Extended exposures with fused gallium dichloride failed to

[4] Delwaulle, *Compt. rend.*, 1955, **240**, 2132.
[5] Bues, *Z. anorg. Chem.*, 1955, **279**, 104.
[6] Hampe, *Jahresber.*, 1888, Part 1, p. 388.
[7] Woodward, *Phil. Mag.*, 1934, **18**, 823.
[8] Gerding, Haring, and Renes, *Rec. Trav. chim.*, 1953, **72**, 78.

show either of these frequencies, though they were at once confirmed with fused gallium trichloride.

From the results we conclude that $GaCl_4^-$ is the preponderant polyatomic species in fused gallium dichloride at 190°, and that under these conditions the compound is to be formulated as gallium(I) tetrachlorogallate (III).

## Experimental

*Preparation of Gallium Dichloride* (cf. Laubengayer and Schirmer [9]).—A weighed amount of pure gallium (supplied by Messrs. Johnson, Matthey & Co.) was converted into the trichloride by passing a stream of pure dry chlorine over the gently heated metal. The trichloride was condensed into a bulb *A* containing a further quantity of gallium, slightly in excess of the calculated weight for the complete reduction of the trichloride to dichloride. To this was connected another bulb, *B*, which was in turn connected to the Raman tube. Bulb *B* was constructed with a long neck. The whole system was evacuated, sealed off, and kept at 180° for 24 hr. with occasional shaking. The product was distilled into the bulb *B*, and bulb *A* was drawn off. The remaining apparatus was placed overnight at 200°, except for a short portion of the long neck of bulb *B*, which was left projecting and was kept cool with an air blast. In this way any excess of gallium trichloride was distilled off from the less volatile dichloride. Finally the pure dichloride was poured *in vacuo* into the Raman tube, which was then sealed off.

As thus prepared, gallium dichloride was an opaque, somewhat waxy, white solid, melting at 165° to a colourless liquid (Found: Ga, 48·9; Cl, 50·7. Calc. for $GaCl_2$: Ga, 49·6; Cl, 50·4%). Similar preparations (Brewer, Garton, *et al.*, unpublished work) consistently yielded specimens containing not more than 3% of $GaCl_3$ as impurity.

*Raman Spectra.*—The technique was that described in the preceding paper.[8] A sodium nitrite filter was used to diminish the intensity of the primary lines of shorter wavelength than 4358 Å.

The sample of gallium dichloride was melted and kept at approx. 190° by a stream of electrically preheated air passing through the annular space between the Raman tube and the surrounding Dewar sleeve. The Raman scattering was intense: with natural incident light the complete Raman spectrum could be photographed on Ilford Zenith plates with an exposure time of only 2 min. Longer times were used in unsuccessful attempts to find additional weaker lines. During the work the sample was allowed to solidify and was remelted several times. No consequent change in the spectrum was observed. In all, the compound was irradiated in the fused state for several hours. No signs of chemical decomposition (such as deposition of gallium metal) were noticeable: the melt was always clear and colourless.

We thank Mr. F. M. Brewer for his interest in this work and for kindly giving us the benefit of his experience with gallium dichloride and related compounds. We are indebted to the Royal Society for a grant (to L. A. W.) with which the spectrograph was purchased. One of us (G. G.) thanks Imperial Chemical Industries Limited for a Research Fellowship, and another (H. L. R.) thanks the D.S.I.R. for a maintenance grant.

Inorganic Chemistry Laboratory, Oxford. [*Received, May 25th, 1956.*]

[9] Laubengayer and Schirmer, *J. Amer. Chem. Soc.*, 1940, **62**, 1578.

## 725. *The Surface Chemistry of Germanium. Part I. Chemical Effects at* pn *Junctions.*

By J. I. Carasso and I. Stelzer.

Deviations in the current–voltage characteristics of reverse-biassed germanium *pn* junction diodes exposed to various environments are summarised. Further observations are reported which suggest a mechanism correlating the electrical effects of the gas on the diode with its chemical properties. The electron affinity (or ionisation potential) of the adsorbate and the work function of the germanium are related to the equilibrium conditions occurring at the surface.

Highly purified germanium at room temperature has been shown to contain equal numbers of conducting electrons and positive holes, which implies that the net concentration of residual donor or acceptor impurities is too small to move the Fermi level from its position mid-way between the bottom of the conduction band and the top of the valency band. By suitable addition of donor (Group V) or acceptor (Group III) impurities an excess of conducting electrons or holes may be introduced. The material is then said to be of the *n*-type or *p*-type respectively. When a transition from *n*- to *p*-type conduction

Fig. 1. *Theoretical characteristic of a* pn *junction.*

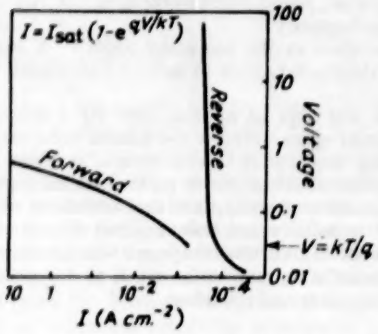
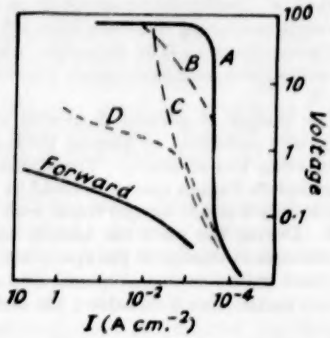



Fig. 2. *Characteristics exhibited by real diodes.*




occurs in an otherwise homogeneous germanium sample the resulting *pn* junction behaves as a rectifier of electric current. This device has been described by Shockley,[1] whose analysis yields the following expression for the dependence on applied voltage of the current flowing across the junction:

$$I = I_{sat}[1 - \exp(qV/kT)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $I$ is the current flowing for a bias $V$ at temperature $T$. The constant $I_{sat}$ is determined by the equilibrium concentrations and lifetimes of minority carriers in the material on both sides of the junction. $I_{sat}$ is very temperature-dependent, but is voltage-independent up to a few tens of volts if the material on at least one side of the junction has a resistivity of 1 ohm cm. or more. It can be seen that the current will saturate at the value $I_{sat}$ for a negative applied bias of a few times $kT/q$, while it will increase indefinitely for a positive applied bias (Fig. 1). Clearly this device is an efficient rectifier.

Germanium *pn* junctions have been made by a variety of methods and found to exhibit current–voltage characteristics in excellent agreement with eqn. (1) up to a voltage at which breakdown phenomena, not considered in the derivation of the equation, set in, provided

[1] Shockley, *Bell Syst. Tech. J.*, 1949, **28**, 435.

their surface is suitably treated after manufacture and suitably protected against subsequent contamination (Fig. 2, curve *A*). Unsuitable surface treatment leads to the types of deviation shown in curves *B*, *C*, and *D* of Fig. 2. From a study of these deviations conclusions can be drawn concerning the mechanism of chemisorption at semiconductor surfaces. It will be shown that anomalous *pn* junction characteristics arise by a mechanism akin to that occurring in heterogeneous catalysis, as described by Dowden.[2]

Deviations of type *B* have been ascribed to the presence of a surface film of water [3] which causes a leakage current approximately proportional to the applied voltage. Law [3] explains this effect in terms of electrolytic surface conduction: he has shown that the excess of reverse current begins to increase appreciably only when the relative humidity reaches the value at which the adsorbed water becomes mobile and that the measured conductance is in good agreement with the value expected from a mass-spectrographic estimation of the surface density of adventitious ions. A number of investigators have however been unable to find any evidence for the mass transfer which should result from

FIG. 3. *Energy-band diagram for an n-type semiconductor with positive surface-space charge.*

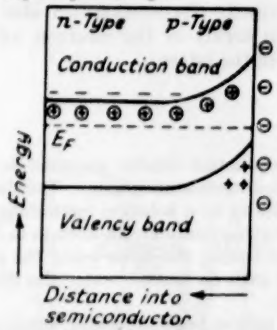
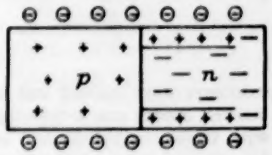



FIG. 4. *Effect of channel formation on rectifying area.*




such a mechanism, and McWhorter [4] concludes that the current is carried by a non-electrolytic process, possibly by electrons jumping from one trap to another in a direction parallel to the surface.

Deviations of type *C* are explained by extending the concept of surface states and space-charge regions which are postulated at the free surface of a semiconductor.[5,6] A model has been developed for the state of affairs at the surface of a *pn* junction covered by an ionic layer. Fig. 3, representing the energy diagram of *n*-type material covered with a layer of negative ions, shows that the presence of such a layer results in the build-up of a positive space-charge near the semiconductor surface, this space-charge consisting predominantly, for small surface densities of ions, of ionised donor centres (not neutralised by mobile electrons). As the surface density of negative ions increases, the concentration of mobile holes near the surface eventually predominates, giving rise to a surface inversion layer which behaves as *p*-type material and is called a "channel." [7] Fig. 4 depicts the increase in the effective rectifying area of a *pn* junction diode resulting from the formation of such a channel. The extra rectifying area has been shown [8] to depend on the applied bias in a way consistent with the commonly observed deviations of the type shown in Fig. 2, curve *C*. A similar argument applies to *n*-type channels on the *p* side. Although

[2] Dowden, *J.*, 1950, 242.
[3] Law, *Proc. Inst. Radio Engineers*, 1954, **42**, 1367.
[4] McWhorter, Massachusetts Inst. Technol., Lincoln Lab. Tech. Report No. 80, May 20, 1955, p. 51.
[5] Bardeen, *Phys. Rev.*, 1947, **71**, 717; Shockley and Pearson, *ibid.*, 1948, **74**, 232; Bardeen and Brattain, *Bell Syst. Tech. J.*, 1953, **32**, 1.
[6] Garrett and Brattain, *Phys. Rev.*, 1955, **99**, 2, 376.
[7] Brown, *ibid.*, 1953, **91**, 518.
[8] Christensen, *ibid.*, p. 1371.
[8] McWhorter and Kingston, *Proc. Inst. Radio Engineers*, 1954, **42**, 1376.

the existence of a channel can be demonstrated unequivocally only by a photoinjection method, as used by Christensen [9] and McWhorter and Kingston,[8] it seems fairly certain that a curve of type *C* must indicate channel formation. No alternative mechanism has been put forward which could account for the shape of this curve, neither have instances been reported of type-*C* curves not caused by channels. Further evidence in support of the assumption made here that atmospheres which cause the reverse characteristic to assume shape *C* do so by inducing channels is provided by experiments on alloy-junction transistors carried out by Mr. F. F. Roberts, of this Station, who found that changes in atmosphere giving rise to type-*C* characteristics also increased the capacitance of the collector and the current gain of the device, demonstrating that the atmosphere under test had caused an increase in the collector area, and therefore a channel.

When surface electrical breakdown phenomena occur in addition to the above mentioned effects curves of type *D* are obtained.

So far only oxygen has been shown [7,8,9] to cause *p*-type channels on the *n* side, and water the opposite type of channel under certain conditions.

In this paper the effect of other oxidising agents, such as nitrogen peroxide and the halogens, is considered, and the behaviour of the diode in the vapours of the ionising solvents ammonia, sulphur dioxide, and water is described. Expressions are also obtained for the equilibria between adsorbate and surface in terms of the electron affinity (or ionisation potential) of the former and work function of the latter.

## Experimental

All experiments were carried out on a set of four junction diodes prepared by alloying indium at 500° on 3 ohm cm. *n*-type germanium in a hydrogen atmosphere. The diodes were degreased with trichloroethylene and etched electrolytically in a solution containing 5·5 g. of sodium hydroxide and 4·0 g. of disodium dihydrogen ethylenediaminetetra-acetate in 100 ml. of distilled water. A current of 5 ma was passed for about 1 min., the diode being the anode and a platinum electrode the cathode. After being rinsed with de-ionised water the diodes were mounted in a borosilicate-glass manifold (Fig. 5).

Atmospheres of pure nitric oxide, nitrogen peroxide, iodine, bromine, water, sulphur dioxide, and ammonia were individually introduced into the manifold.

*Nitric Oxide.*—The crude gas was generated from nitric acid (*d* 1·20) and copper and collected in cold saturated aqueous ferrous sulphate. Flask *R* containing the $FeSO_4$,NO complex was joined to the purifying system (Fig. 6). Nitrogen was blown through the whole system, including the manifold, to displace most of the air present. Tap *G* was then closed and the system was evacuated to about 30 μm. Tap *H* was closed and *G* opened so that nitrogen again filled the apparatus. Evacuation was repeated, and finally water was drawn up into *M* by closing *K* and *L* and manipulating *G*. The system was evacuated to 10 μm. and taps *E*, *D*, and *H* were closed. The characteristics of each diode could then be measured in a vacuum. Tap *L* was next opened and the $FeSO_4$,NO solution slowly warmed so that nitric oxide collected in reservoir *M*. When sufficient nitric oxide had been generated, *L* was shut and the gas slowly admitted into *I* by opening *G* and *F*, the pressure being noted on the manometer *J*. Flask *I* contained nitric oxide, a trace of nitrogen, and some moisture. Nitrogen has been shown to have no effect on germanium *pn* junctions;[10] the water was frozen out by the trap *O* at −80°. Known amounts of pure nitric oxide could thus be introduced into the manifold *via* the taps *E* and *D*, which were used as a gas pipette.

*Nitrogen Peroxide.*—Lead nitrate was heated electrically in a slow stream of oxygen and the gases were passed over lead peroxide and phosphoric oxide into a trap at −20°. From this, nitrogen peroxide was sublimed under reduced pressure into a trap at −80°. This was connected to the manifold at *D* and used as a source of nitrogen peroxide. The pressure of nitrogen peroxide in the system was controlled by the use of suitable cooling agents, after the system had been evacuated with the cold trap at −180°, and sealed off at *B*.

*Bromine.*—Owing to the absorption of bromine by tap-grease it was necessary to work in a tap-free apparatus. The system was sealed off at the constriction *A* (Fig. 5) and outgassed by prolonged pumping. The vacuum was released and the end *P* opened. Some drops of bromine

[10] Law and François, *Ann. N.Y. Acad. Sci.*, 1954, **58**, 925.

were introduced into the tube *C*, which was surrounded by liquid air, and the tube was quickly sealed at the constriction *Q*. The system was evacuated with the liquid-air trap in position and sealed off at the constriction *B*. The vapour pressure of bromine in the diode enclosure could be controlled by suitable choice of the freezing agent around *C*.

*Iodine.*—A technique similar to that for bromine was used.

*Water.*—A small flask of distilled water was sealed on to the manifold, and the pressure of water vapour allowed into the evacuated system was controlled by a gas-pipette and measured on an oil-manometer.

*Sulphur Dioxide.*—After the system had been outgassed by prolonged pumping, commercial sulphur dioxide (A. Boake Roberts and Co.) was admitted to 1 atm. pressure and the system was

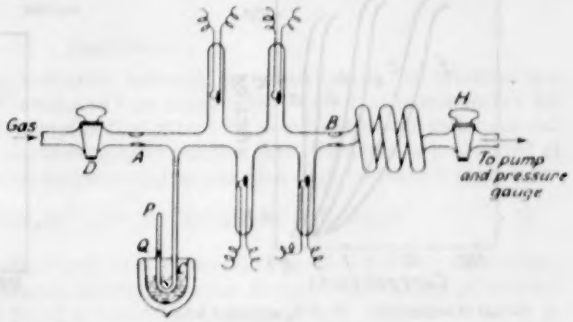



FIG. 5. *Manifold and cold finger.*

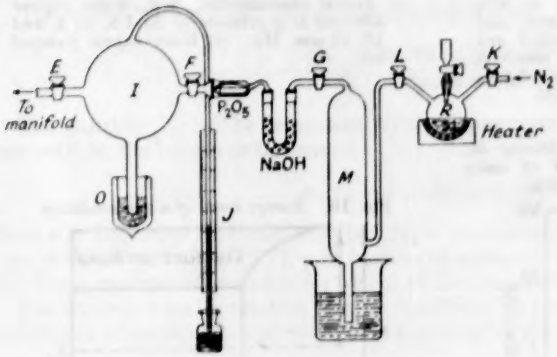



FIG. 6. *Purification of nitric oxide.*

closed. The concentration of sulphur dioxide could be varied by placing limb *C* in cooling baths of various temperatures.

*Ammonia.*—Pure dry ammonia, obtained from a gas cylinder (Anhydrous Ammonia Co.), was introduced into the system. The concentration was again controlled by freezing.

## RESULTS

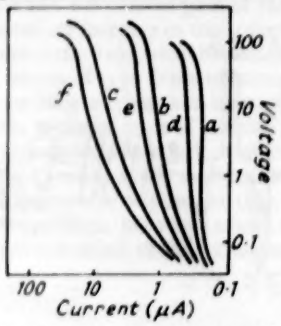
The diodes were exposed to each ambient gas in turn, over a range of pressures, and their characteristics were observed, d.c. from a high-impedance source being used. Some time effects were observed in the experiments with ionising solvents, especially in the region of the characteristic where the power dissipated was sufficient to " boil off " the adsorbed layers, but not in the experiments with oxidising atmospheres. With nitrogen peroxide, bromine, and iodine it was expedient to pump or freeze off the excess of gas to avoid excessive attack on the device. This was thought permissible because equilibrium chemisorption was almost instantaneous and practically irreversible for any particular gas-pressure. For the other atmospheres, however, equilibrium conditions had to be maintained throughout, because reversibility was observed.

Nitric oxide, purified as described, has a negligible effect on the diodes. Less carefully

purified nitric oxide caused a definite channel, which we ascribe to the presence of traces of nitrogen peroxide.

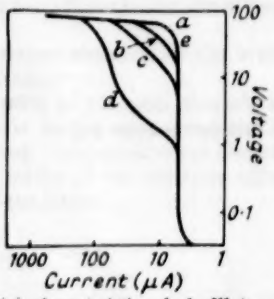
Nitrogen peroxide and bromine were used in succession. Nitrogen peroxide was allowed into the manifold; the non-chemisorbed gas was pumped off, the characteristics were observed, and the experiment was then repeated for a higher initial pressure of nitrogen peroxide. Air was allowed into the apparatus, the system was again evacuated, and the bromine was introduced. Curves of the type shown in Fig. 7 were obtained for such a cycle. It can be seen that both

FIG. 7. *Reverse characteristics for the nitrogen peroxide–moist air–bromine cycle.*



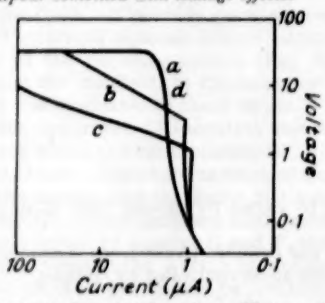

*a, Initial characteristic. b, $NO_2$ admitted from source at −80° and pumped off. c, $NO_2$ admitted from source at room temp. and pumped off. d, Moist air admitted and pumped off. e, Br admitted from source at −180° and pumped off. f, Br admitted from source at room temp. and pumped off.*

FIG. 8. *Reverse characteristics showing the reversible leakage effect induced by water vapour.*



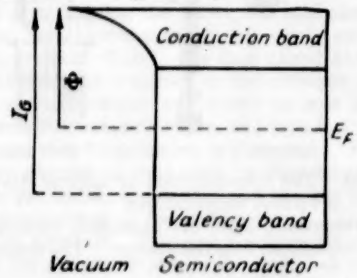

*a, Initial characteristic. b–d, Water vapour admitted to a pressure of (b) 1·5, (c) 4, and (d) 10 mm. Hg. (e) Water vapour pumped off.*

FIG. 9. *Reverse characteristics showing the reversible "anti-channel" effect of water vapour combined with leakage effects.*




*a, Initial characteristic. b, c, Water vapour admitted at (b) 2, (c) 6 mm. Hg. d, Water vapour pumped off.*

FIG. 10. *Energy levels of a semiconductor.*




reagents produce channels whose magnitude depends on the initial concentration of the gas; further, both reagents slightly raise the voltage at which breakdown occurs.

Iodine behaves similarly to bromine, with regard to both channel formation and raising of the breakdown voltage.

With originally channel-free diodes, water gives no apparent new channels under our experimental conditions, but a reversible leakage effect resulting in a family of curves of type *B* (Fig. 8). If a channel, of unknown origin, resulting from incorrect surface treatment, is initially present, and the diode is exposed to water vapour, some of the channel is cancelled (Fig. 9) while the upper part of the curve becomes of type *B*. For a very large initial channel it

becomes difficult to distinguish between the various types of phenomena. In addition to these effects a large pressure of water vapour lowers the breakdown voltage.

The failure of water vapour to cause *n*-type channels to appear on the *p* side of our (alloy) junctions does not conflict with the findings of Brown [7] and others,[8, 9] and is due to the very heavy doping of our *p*-type material (estimated to be of the order of $10^{19}$ indium atoms per cm.$^3$). The " grown " junctions upon which water has been shown to induce channels were made with *p*-type material of acceptor density about $10^{15}$ cm.$^{-3}$.

Sulphur dioxide behaves similarly to water in that it cancels channels and gives a family of curves of type *B*. In addition, there is a tendency to raise the breakdown voltage.

Anhydrous ammonia behaves similarly to water and sulphur dioxide, except that the breakdown voltage seems to be completely unaffected.

## Discussion

It seems probable, from the similarity between our observations on bromine and nitrogen peroxide, and those of Christensen [9] on oxygen, that oxidation is responsible for the channel effects observed. This implies that attack by neutral atoms or molecules can result in channel formation. An electron-transfer reaction must therefore be postulated at the semiconductor surface, such as that represented by eqn. (2) for *p*-type channel formation :

$$\mathrm{X\ (on\ surface)} + \mathrm{Surface} \overset{+}{-} \rightleftharpoons \mathrm{X^-\ (on\ surface)} + \mathrm{Surface^+} \quad . \quad . \quad (2)$$

where X is the adsorbate and Surface$^+$ indicates an excess of positive holes at the surface. This equation, which we have deduced directly from the accepted mechanism of channel formation [5, 7] is in agreement with Dowden's model of chemisorption.[2]

The equilibrium constant for this reaction is given by :

$$K = \frac{[\mathrm{X^-}][\text{positive holes at surface}]}{[\mathrm{X}][\text{electrons at surface}]}$$

The quantity [X] will be determined by the appropriate isotherm, which in the simplest case could be the Langmuir isotherm :

$$n/N_0 = \theta = kp/(\nu + kp)$$

where $n$ = number of molecules adsorbed, $N_0$ = number of molecules in the complete monolayer, $k = 10^{22} \times 3{\cdot}5\gamma/\sqrt{(MT)}$, $\gamma$ = fraction of molecules which condense on striking, $\nu$ = rate of evaporation, $M$ = molecular weight of the gas, and $T$ = absolute temperature.

The electron-transfer reaction may be considered to produce a homogeneous electronic equilibrium whose equilibrium constant is governed by the relation

$$-\Delta G = \boldsymbol{R}T \ln K$$

where the standard states are given as 1 mole of $\mathrm{X^-}$ (containing $\boldsymbol{N}$ electrons where $\boldsymbol{N}$ is Avogadro's number), 1 mole of X, $\boldsymbol{N}$ electrons at the surface and $\boldsymbol{N}$ holes at the surface. There must be no movement of atoms or molecules into or out of the surface. In such a case an estimation of $-\Delta G$ can be made in terms of the electron affinity of X and the work function of the semiconductor, which will determine the distribution of the electron " gas " between X and the surface.

The electron affinity ($\alpha$) of X is defined as the energy liberated when an electron is put into the neutral molecule. This will be the energy change occurring when an electron is brought from infinity into the lowest unoccupied orbital of X. The isothermal work function ($\Phi$) of a solid is usually defined as the energy required to move an electron from the Fermi level $E_F$ to infinity (Fig. 10), whereas the adiabatic work function $I_G$ would be measured from the top of the valency band. Since experimental conditions are usually isothermal $\Phi$ will apply. This uncertainty regarding the level from which to measure the energy does not arise in the case of the adsorbate, X, because atoms and molecules undergo no appreciable excitation from bonding to antibonding orbitals at room temperature.

The change in free energy in going from reactants to products must be given by $\Phi - \alpha$, in which case

$$-(\Phi - \alpha)N = RT \ln K_-$$

It can be seen that if $\alpha$ is large there will be considerable channel formation; further, if [X] becomes large because the gas pressure is increased there will again be an increase in channel formation. From a knowledge of [X] (*via* the appropriate isotherm) and of the free-energy change it becomes possible to estimate the number of negative ions which have been formed on the surface.

A similar treatment can be applied to the electron-transfer reaction (3) which would give an *n*-type channel on the *p* side :

$$X + \text{Surface} \rightleftharpoons X^+ + \text{Surface}^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

in which case the free energy change is given by $\beta - \Phi$, and

$$-(\beta - \Phi)N = RT \ln K_+$$

where $\beta$ is the ionisation potential of X. If $\beta$ is large compared with $\Phi$ there will be little chemisorption, and consequently slight channel formation. We have in fact found no evidence of *n*-type channel formation by nitric oxide, in spite of the known stable existence of the nitrosonium ion $NO^+$, in agreement with expectations from published values for its ionisation potential. This is given [11] as 9·5 ev which is much higher than the work function [12] of germanium, 4·8 ev, giving a very small stability constant for reaction (3). The adsorption isotherms of the adsorbates discussed must be determined before the validity of these equations can be fully tested by comparing the electron affinities (or ionisation potentials) and surface concentrations of adsorbates with their channel-forming powers. It has however been observed that the effect of halogens is much greater than that of nitrogen peroxide. This is to be expected from these considerations, since the halogens have a much larger electron-affinity than nitrogen peroxide.

The similarity in the results obtained by using water, sulphur dioxide, or ammonia suggests that ionising solvents are responsible for the production of curves of type *B* (Fig. 2). It is possible that these merely solvate the ions which are present on the surface, as implied by Law.[3] If such ions are also responsible for channel formation, solvation would automatically reduce the electrostatic effect of the negative or positive ions, which maintain, respectively, the positive or negative space-charge in the vicinity of the surface, because each ion becomes surrounded by a sheath of solvent molecules which effectively screen its charge in addition to increasing its distance from the germanium surface. This mechanism could therefore explain the cancellation of channels by ionising solvents which we have observed (see Fig. 9). Complete removal of the solvent usually results in the reappearance of the channel, which is also not unexpected on the basis of this solvation mechanism. The irreversible removal of the nitrogen peroxide channel by moist air, reported here, is however difficult to explain in these simple terms, and probably involves chemical reaction between the chemisorbed nitrogen peroxide and the adsorbed water.

We are grateful to our colleagues, Mr. F. F. Roberts and Mr. G. T. Hollins, for much helpful discussion, also to the Engineer-in-Chief of the General Post Office, and to the Controller of Her Majesty's Stationery Office, for permission to publish this paper.

Post Office Engineering Research Station, Dollis Hill, London, N.W.2.
Queen Mary College, Mile End Road, London E. [*Received, February 1st*, 1956.]

[11] Tate, Smith, and Vaughan, *Phys. Rev.*, 1935, **48**, 525; Hagstrum and Tate, *ibid.*, 1941, **59**, 354.
[12] Wright, *Proc. Inst. El. Engineers*, 1953, **100**, 111, 125; Law, *J. Phys. Chem.*, 1955, **59**, 543.

# 726. *The Mesomorphic Behaviour of the Fatty Esters of Cholesterol.*

By G. W. Gray.

Fourteen fatty esters of cholesterol have been prepared, and their m. p.s and mesomorphic transition temperatures determined. These new values are compared with constants already recorded, and the differences discussed in terms of purity and method of determination of the transition points. The number of phases exhibited by these esters is discussed, and a probable resolution of the disagreement about this number expressed in previous publications has been reached. A brief comment has been made on the nature of the cholesteric phase, such that, although it may best be regarded as an individual phase type, it is more similar to the smectic than to the nematic mesophase.

The phenomenon of mesomorphism was first discovered by Reinitzer,[1] who observed that cholesteryl benzoate melts at 145·5° to form a cloudy, viscous melt, which on further heating is transformed into the isotropic liquid at 178·5°. It is now recognised that the ester exhibits a cholesteric phase, and Reinitzer's observation was soon followed by the preparation of many organic compounds which exhibit mesomorphism. It soon became evident that most mesomorphic compounds have phases of either the smectic or nematic type, and that cholesteric phases are found exclusively in derivatives of cholesterol or in molecules of a similar shape or constitution. The cholesteric phase is therefore less common, but, despite this, its characteristic properties have been very carefully examined by Friedel.[2]

In recent publications[3] which relate to the effects of molecular constitution on mesomorphic behaviour, twenty-one series of alkoxyarenecarboxylic acids and alkoxybenzylidenearylamines have been described. When the mesomorphic transition temperatures for any one of these series are plotted against the number of carbon atoms in the alkyl chain, it is found that smooth curves may be drawn through the points for like transitions. Thus, in a series which exhibits both smectic and nematic phases, the nematic–isotropic transition points lie on two smooth, falling curves, dependent on whether the number of carbon atoms in the alkyl chain is even or odd, whilst the smectic–nematic points constitute a rising curve, which, at or near its maximum, joins the nematic–isotropic transition point curve. On the other hand, the *n*-propyl 4′-*n*-alkoxydiphenyl-4-carboxylates,[4] which show only smectic phases, give smectic–isotropic transition points which again lie on two curves, but these rise to a maximum early in the series, before falling, steeply at first and then more gradually, as the alkyl chain is lengthened. Because of this characteristic behaviour of smectic–nematic, nematic–isotropic, and smectic–isotropic transition points of homologous series, it would seem reasonable to expect that transitions involving the cholesteric phase would behave similarly and lie on smooth curves. Cholesteryl esters of the normal, open-chain, fatty acids afford an opportunity to verify this, and the transition temperatures of several esters of low and high molecular weight have been reported by Jaeger [5] and Friedel,[2] respectively. If their transition temperatures (solid–cholesteric, smectic–cholesteric, and smectic– or cholesteric–isotropic) are plotted against the number of carbon atoms in the alkyl chain, it is found that a smooth curve cannot be drawn through the points. It is significant too that Jaeger and Friedel quote widely different constants for cholesteryl decanoate. Moreover, Friedel,[2] Lehmann,[6] and Jaeger [5] disagree about the number and nature of the phases which they observed in several cholesteryl esters. Table 1 summarises the information available for twelve cholesteryl esters. Monotropic transition temperatures are in parentheses.

[1] Reinitzer, *Monatsh.*, 1888, **9**, 435.
[2] Friedel, *Ann. Physique*, 1922, **17**, 273.
[3] Gray, Brynmor Jones, *et al.*, *J.*, 1955, 4359, and preceding parts.
[4] Gray, Hartley, and Brynmor Jones, *J.*, 1955, 1412.
[5] Jaeger, *Rec. Trav. chim.*, 1906, **25**, 334.
[6] Lehmann, *Z. phys. Chem.*, 1906, **56**, 750.

A re-examination of the mesomorphic properties of the fatty esters of cholesterol is obviously necessary in view of these disagreements and the incompleteness of the available information. The twelve esters in Table 1, together with cholesteryl heptanoate and palmitate, have therefore been prepared, and their transition temperatures (solid–cholesteric or smectic, smectic–cholesteric, and cholesteric–isotropic) are summarised in Table 2, where monotropic transitions are in parentheses, and, with the exception of the temperatures for the formate, are plotted against the number of carbon atoms in the ester alkyl chain in the Figure.

In nearly all cases, the constants given in Table 2 are higher, by 1—9°, than those reported by Jaeger (Table 1). These variations may be attributed to impurity in Jaeger's esters, since it is unlikely that these would be prepared from the highly pure materials, such as are now commercially available. In only two cases have lower transition temperatures been recorded, and these involve the monotropic cholesteric–isotropic transition points for cholesteryl formate and octanoate. Jaeger's method for determining monotropic transitions involved very sudden chilling of the isotropic liquid, and it is probable that the thermometer was not at equilibrium with the supercooled melt. The recorded constants

TABLE 1.

| Cholesteryl ester | Temp. of transition to: smectic | cholesteric | isotropic | Ref. | Number of phases: Friedel | Lehmann |
|---|---|---|---|---|---|---|
| Formate | — | (*ca.* 90°) | 96·5° | 5 | 1 | 1 |
| Acetate | — | (80—90°) | 112·8 | 5 | 1 | 2 |
| Propionate | — | 93° | 107·2 | 5 | 1 | * |
| Butyrate | — | 96·4 | 107·3 | 5 | 1 | 2 |
| Valerate | — | 91·8 | 99·2 | 5 | 1 | 2 |
| Hexanoate | — | 91·2 | 100·1 | 5 | * | 2 |
| Octanoate | — | (*ca.* 101) | 106·4 | 5 | 2 | 2 |
| Nonanoate | 78° | 79 | 90·5 | 2 | 2 | * |
| Decanoate | —<br>55·5 | 82·2<br>68·5 | 90·6<br>85 | 5<br>2 | 2 | 2 |
| Laurate | 79 | 81 | 88 | 2 | 2 | 3 |
| Myristate | 72 | 78 | 83 | 2 | 2 | 3 |
| Stearate | monotropic | — | ? | 2 | 1 | * |

* Not examined.

TABLE 2.

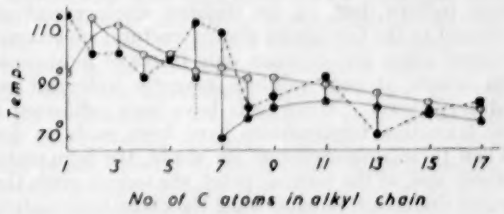
| Cholesteryl ester | Temp. of transition to: smectic | cholesteric | isotropic | Cholesteryl ester | Temp. of transition to: smectic | cholesteric | isotropic |
|---|---|---|---|---|---|---|---|
| Formate | — | (60·5°) | 97·5° | Octanoate | (69·5) | (96·5) | 110 |
| Acetate | — | (94·5) | 116·5 | Nonanoate | (77·5) | 80·5 | 92 |
| Propionate | — | 102 | 116 | Decanoate | (81·5) | 85·5 | 92·5 |
| Butyrate | — | 102 | 11[illegible] | Laurate | (83·5) | (90) | 93 |
| Valerate | — | 93 | 101·5 | Myristate | 71 | 81 | 86·5 |
| Hexanoate | — | 99·5 | 101·5 | Palmitate | (78·5) | 79 | 83 |
| Heptanoate | (<92·5°) | (95·5) | 114 | Stearate | (75·5) | (79·5) | 83 |

would then be too high to an extent dependent on the rate of cooling necessary to produce the mesophase before crystallisation occurred.

Friedel's constants (Table 1) are also, in general, lower than the present values, and in cholesteryl decanoate the difference is very great. Jaeger too records transition temperatures for this compound which are widely different from Friedel's. Impurity in Friedel's ester may again explain these discrepancies, and it is significant that he reports the presence of crystalline material in the cholesteric phases of cholesteryl laurate and myristate. Friedel explains this effect in terms of high-melting polymorphic modifications, but it is more likely that the crystals were high-melting impurity.

Despite these variations from previously recorded values, it is felt that the constants in Table 2 are accurate and reliable, since the specimens used appeared to be pure as indicated by the combustion analyses and the sharp, clear-cut reversibility of the isotropic–cholesteric and cholesteric–smectic transitions. Added confidence is given by the smooth

curve relations shown by the transition temperatures in the Figure. Thus, the smectic–cholesteric points lie on one curve which rises at first and then falls gradually, with a maximum at cholesteryl laurate. This curve is similar to smectic–nematic curves observed in other homologous series, but it is noteworthy that, whereas in most of these cases nematic properties do not exist in the last two or three members of the series, here cholesteric phases persist in all the long-chain esters examined. The cholesteric–isotropic transitions lie on two curves, of which the lower falls steeply at first and then more gradually through the points for esters with an even number of carbon atoms in the alkyl chain. However, the upper curve, for the esters with an odd number of carbon atoms in the chain, rises steeply from the acetate to the butyrate, and then falls gradually through the points for the hexanoate, octanoate, decanoate, laurate, myristate, palmitate, and stearate. The first section of this curve cannot be drawn accurately, but the significant feature is that the curve does show a maximum. This immediately recalls the smectic–isotropic curves for the *n*-propyl 4′-*n*-alkoxydiphenyl-4-carboxylates [4] which behave similarly. It was suggested that this behaviour in the diphenyl esters may be due to their very weak terminal intermolecular cohesions compared with the lateral and planar cohesions, and similar factors may operate in the cholesteryl esters. This cannot at present be confirmed however. If the cholesteric–isotropic transition point for cholesteryl formate were included in the Figure and considered as the origin of the curve for the esters with an even number of carbon atoms in the chain (zero being considered as an even number), this curve too would




rise at first and have a maximum at the propionate. This point has not been included in the Figure, since the terminal cohesions arising from the formate grouping will not be comparable with those originating from groups with even-number carbon chains. However, the other cholesteric–isotropic curve is so similar to the smectic–isotropic curve for the diphenyl esters that it is a logical step to relate cholesteric– and smectic–isotropic transitions, and to consider whether the cholesteric phase may not simply be a polymesomorphic modification of the smectic phase. This point of view is strengthened by other features which the two phases have in common—both phases appear from the isotropic liquid in characteristic bâtonnets which coalesce to form focal-conic groups arising from layer structures in the mesophases. On the other hand, definite differences do exist, and whilst the smectic phase is optically positive, the cholesteric phase is optically negative and has other distinctive properties (intensely iridescent coloration, high optical-rotatory power) which are not found in smectic phases. At any rate, the cholesteric phase appears to be more closely related to the smectic phase than it is to the nematic phase, which gives no bâtonnets or focal-conic groups, is optically positive, and has no iridescence or optical-rotatory power. Despite this, Friedel asserted that the cholesteric phase is nematic in type, but he based his arguments entirely upon the fact that he had never observed more than one smectic phase in a given compound, and that the smectic phase is most commonly found in conjunction with the nematic phase. Since cholesteryl esters exhibit smectic phases at lower temperatures and cholesteric phases at higher temperatures, he concluded that the latter are of nematic type. Friedel's reasoning can no longer be considered valid, because polymesomorphism [7] is now well established, and many compounds, *e.g.*, the 6-alkoxy-5-nitro-2-naphthoic acids [8] and the 4′-alkoxy-3′-nitrodiphenyl-4-carboxylic

[7] Vorländer, *Trans. Faraday Soc.*, 1933, **29**, 913; Bernal and Crowfoot, *ibid.*, p. 1032.
[8] Gray and Brynmor Jones, *J.*, 1955, 236.

acids,[9] exhibit two or even three smectic-type phases. Moreover, the smectic–cholesteric transition point curve is similar in shape, not only to smectic–nematic curves, but also to smectic–smectic transition point curves, which also have a maximum. It is quite possible then to regard the cholesteric phase as being smectic in type, but as possessing additional characteristics which arise from the particular molecular structure of cholesteric compounds and not necessarily from the manner of orientation of these molecules relative to one another in the mesophase. However, until the molecular orientation in the cholesteric phase is known precisely, it is best to classify the mesophase as a distinct phase type, but, if this is indeed the case, its properties are more similar to those of the smectic phase, and the shape of the cholesteric–isotropic transition point curve in the Figure is an added feature which relates the phases to one another.

A further feature of the results in Table 2 is that the first six esters exhibit only one phase (cholesteric) and the remainder two phases (smectic and cholesteric). With the exception of cholesteryl stearate, these facts agree with Friedel's observations, but in several cases Lehmann [6] reports the existence of an additional phase. It seems possible to explain these discrepancies in terms of the appearances which the cholesteric phase may adopt on a glass supporting surface. If a sample of one of these esters is melted on a glass slide and pressed down under a cover slip to obtain a thin section, observations on the number and the appearance of the phases can readily be made visually or by means of a microscope with crossed nicols, while the specimen is heated or cooled. According to Friedel, the cholesteric phase appears from the isotropic liquid in bâtonnets which coalesce to a focal-conic pattern, but, on the slightest displacement of the cover slip, this is immediately changed to the Grandjean plane structure, which consists of large homogeneous areas with stepped edges and contains only traces of focal-conic groups. When this change occurs, the sample at once exhibits intensely iridescent colours and exceedingly high optical-rotatory power. These facts have been confirmed in this study, and determinations of the transition temperatures have been made as described in the experimental section. When these measurements are made, the temperature of the mounted sample is slowly raised, and, at the melting point, the sample gives the focal-conic cholesteric phase, which, unless disturbed, remains until the cholesteric–isotropic transition temperature is reached, and the field of view between crossed nicols then becomes extinct. From previous experience all nematic– and smectic–isotropic transition temperatures have been found to be precisely reversible within the limits of experimental error, and it was expected that the cholesteric–isotropic transition would behave similarly. When the isotropic liquid is cooled, however, the bâtonnets and focal-conic groups appear at a lower temperature than the cholesteric–isotropic transition, except in cholesteryl formate where the two values are coincident. The extent of this variation between the two temperatures is shown in Table 3.

TABLE 3.

| Ester | Temp. *A* * | Temp. *B* * | Diff. | Ester | Temp. *A* * | Temp. *B* * | Diff. |
|---|---|---|---|---|---|---|---|
| Formate ..... | 60·5° | 60·5° | 0° | Octanoate ..... | 96·5° | 89° | 7·5° |
| Acetate ..... | 94·5 | 93·5 | 1 | Nonanoate ..... | 92 | 91 | 1 |
| Propionate ..... | 116 | 115 | 1 | Decanoate ..... | 92·5 | 88·5 | 4 |
| Butyrate ..... | 113 | 112 | 1 | Laurate ..... | 90 | 87·5 | 2·5 |
| Valerate ..... | 101·5 | 100·5 | 1 | Myristate ..... | 86·5 | 83 | 3·5 |
| Hexanoate ..... | 101·5 | 100 | 1·5 | Palmitate ..... | 83 | 80·5 | 2·5 |
| Heptanoate ..... | 95·5 | 93·5 | 2 | Stearate ..... | 79·5 | 76·5 | 3 |

* Temp. *A* = temperature of focal-conic cholesteric–isotropic transition.
Temp. *B* = temperature of isotropic–focal-conic cholesteric transition.

The isotropic–cholesteric transition temperatures given in Table 3 are average values, since, unlike the cholesteric–isotropic transition temperature which is reproducible to 0·2°, these transitions may vary over 1° in a series of measurements. The differences between the two temperatures vary irregularly along the series between 0° and 7·5°, although the larger differences tend to occur with the longer-chain esters. At first it was thought that supercooling of the cholesteric phases caused this irregular behaviour, although

[9] Gray, Brynmor Jones, and Marson, unpublished work.

this effect has never been found in smectic or nematic phases. The following observations, however, rule out this possibility. If the isotropic liquid obtained from cholesteryl formate is cooled on a slide and observed visually, the phase appears as a light grey wave-front, which, on examination under a microscope between crossed nicols, is seen to consist of bâtonnets and focal-conic groups. A similar set of observations on an ester such as cholesteryl octanoate shows that the phase appears as a dull, blue-grey, opaque wave-front which is well-defined to the eye, but is optically extinct between crossed nicols. On further cooling, a much less well-defined wave-front appears. This is translucent to the eye, but in fact consists of minute focal-conic groups. This behaviour was found in all esters except the formate, which gives no discrepancy between the cholesteric–isotropic and isotropic–cholesteric transition temperatures. With this exception then, the cholesteric phase appears from the isotropic liquid in a completely homœotropic condition, and the focal-conic groups appear at a lower temperature. The values given in the column headed Temp. *B* in Table 3 are therefore in fact homœotropic cholesteric–focal-conic cholesteric transition temperatures. The temperature at which the homœotropic cholesteric phase appears is in all cases the same as that at which the focal-conic cholesteric–isotropic transition occurs. That both the homœotropic and focal-conic conditions are cholesteric in type is shown by the fact that cover-slip displacements give the Grandjean plane structure in each case. Moreover, if the homœotropic phase is converted into the Grandjean structure before the development of focal-conic groups begins, these groups never appear on further cooling. The two wave-fronts were also observed by Lehmann who considered that the homœotropic and focal-conic conditions represented two distinct mesophases. It seems doubtful whether this is a legitimate conclusion, because the homœotropic to focal-conic cholesteric transitions are not exactly reproducible, the distribution of the transition points is irregular along the homologous series of esters, and the invasion of the homœotropic state by the focal-conics is a slow process, often incomplete at a much lower temperature when the smectic phase appears. Further, the change is irreversible and the focal-conic structure passes directly to the isotropic liquid on heating of the sample. This is quite unlike polymesomorphic changes in other systems which have been examined,[8,9] and until more data concerning this change are available, it would seem best to consider the presence of only one cholesteric phase, which may adopt a homœotropic or a focal-conic texture, depending on the molecular orientation on the glass surface and the way in which this orientation changes with falling temperature.

In Lehmann's observations we therefore find that cholesteryl acetate to cholesteryl hexanoate are described as having two phases. Friedel reports that cholesteryl octanoate and decanoate show a smectic and a cholesteric phase, whereas the two phases observed in these esters by Lehmann, who did not detect the smectic phase, are the homœotropic and focal-conic cholesteric modifications. The presence of a smectic phase in the octanoate and decanoate has been fully substantiated in this investigation. In cholesteryl laurate and myristate, where Lehmann did observe smectic properties, he therefore reports three phases—homœotropic cholesteric, focal-conic cholesteric, and smectic.

Friedel makes no reference to this homœotropic condition of the cholesteric phase. It is quite possible that he did not notice its existence, particularly if he examined the phases only under a microscope where the homœotropic state is not visible. This would also explain why he does not record a cholesteric phase for cholesteryl stearate, for, as shown by the values in Tables 2 and 3, the temperature falls to within 1° of the cholesteric–smectic transition point before focal-conic groups begin to develop in the specimen. If the homœotropic state had not been observed, it would be easy to confuse this development of the groups with the appearance of the smectic phase itself.

The above facts seem to account for the differences in the number of phases observed by Friedel and Lehmann in the cholesteryl esters, and also to explain discrepancies between their conclusions and those reached in the present study.

The iridescent colours which are seen when the Grandjean plane structures of cholesteric phases are observed between crossed nicols have been discussed in detail by Friedel,[2] who noticed that the reflected light may vary from infrared to ultraviolet, and changes with temperature. In the cholesteryl esters the wavelength of the reflected light increases as

the temperature falls, and in most cases a greater or lesser part of the solar spectrum is traversed. In this examination, it has been further observed that the wavelength of the reflected light appears to depend also on the length of the ester alkyl chain. For example, the acetate reflects light of colour changing from green to red as the temperature falls, the propionate from violet to yellow, whilst the butyrate to decanoate reflect in the visible violet or at the most in the blue region of the spectrum. Of the above esters, the octanoate, nonanoate, and decanoate exhibit smectic behaviour, and when this phase appears it is preceded by a narrow rainbow in which the solar spectrum is completed, *i.e.*, from blue to red. This effect may be caused by disturbance of the Grandjean planes as they change to the focal-conic smectic state. In cholesteryl laurate to stearate, a further shift to shorter wavelengths is noticeable, for their cholesteric phases reflect no visible colour—the reflected light is presumably ultraviolet. These esters also exhibit smectic phases, but no rainbow effect precedes this phase's appearance. It would appear that in these esters, the disturbances involved in the orientation changes are unable to bring the wavelength of the reflected light into the visible part of the spectrum. The opposite of this is observed in cholesteryl formate. This ester reflects no visible colour of light from its cholesteric phase, but here the wavelength of the reflected light is probably in the infrared region. Cover-slip displacements caused the appearance of flashes of red reflected light.

All compounds which exhibit cholesteric phases behave in this general way, but some may show the reverse sequence of colour changes as the temperature falls, *i.e.*, changing from long to short wavelengths.

## Experimental

*Determination of Transition Temperatures.*—The m. p.s and mesomorphic temperatures of the cholesteryl esters were determined by using the microscope heating block [10] in conjunction with the projection system already described.[11] When observed microscopically between crossed nicols, the cholesteric phases are seen to consist of focal-conic groups of very variable size and definition, whilst the smectic phases are mosaics of minute focal-conic groups which have a marked tendency to become homœotropic. Such detail is not seen when the projector is used, but the difference between the images obtained from the two phases is perfectly distinct. In the case of enantiotropic transitions, the sequence of changes is, therefore, solid–smectic–focal-conic cholesteric–isotropic. On cooling, the isotropic–homœotropic cholesteric phase change is not visible when either projector or microscope is used, and this transition was obtained by visual observation of the mounted sample in the heating block. The temperature at which the focal-conic groups first appear on the screen is readily observed, as is the reversal to the smectic phase at a temperature exactly the same as that obtained on heating the sample. The sequence of changes on cooling is isotropic–homœotropic cholesteric–focal-conic cholesteric–smectic–solid. Monotropic transitions were determined by gradually cooling the specimen until the transition occurred. If supercooling was sufficient, the temperature was then slowly raised to obtain the reversal. The temperatures were coincident in all cases. The usual accuracy ($\pm 0{\cdot}25°$) can be claimed for all transitions, except those of the type homœotropic cholesteric–focal-conic cholesteric, which, as described in the discussion, are not quite reproducible, and average values have been quoted.

*Preparation of Materials.—Cholesteryl formate.* Pure cholesterol (1·0 g.) and 90% w/w formic acid (*d* 1·2; 50 ml.) were heated at 100° for 3 hr. The solution, together with some oil which separated, was poured into water (50 ml.), and the solid filtered off. The ester was crystallised from glacial acetic acid and ethanol until the transition temperatures were constant.

*Cholesteryl acetate—cholesteryl hexanoate.* Cholesterol (1·9 g.), pyridine (20 ml.), and the pure acid anhydride (2 mols.) were heated at 100° for 2 hr. The liquors were poured into water (50 ml.) and the solid filtered off, washed with dilute hydrochloric acid, and crystallised from glacial acetic acid and ethanol until no variation in the transition temperatures was observed.

*Cholesteryl heptanoate—cholesteryl stearate.* Pure acid anhydrides were not available for the preparation of these esters. The pure acids were converted into the acid chlorides by thionyl chloride, and distilled twice. Cholesterol (1·9 g.), redistilled *NN*-dimethylaniline (15 ml.), and the acid chloride (2 mols.) were heated at 100° for 1 hr., oily esters separating. The mixture

[10] Gray, *Nature*, 1953, **172**, 1137.
[11] Gray and Ibbotson, *Nature*, 1955, **176**, 1160.

| Cholesteryl ester | Found C, % | Found H, % | Formula | Calc. C, % | Calc. H, % |
|---|---|---|---|---|---|
| Formate | 81·15 | 11·2 | $C_{28}H_{46}O_2$ | 81·2 | 11·1 |
| Acetate | 81·2 | 11·2 | $C_{29}H_{48}O_2$ | 81·3 | 11·2 |
| Propionate | 81·5 | 11·3 | $C_{30}H_{50}O_2$ | 81·45 | 11·3 |
| Butyrate | 81·5 | 11·4 | $C_{31}H_{52}O_2$ | 81·55 | 11·4 |
| Valerate | 81·7 | 11·6 | $C_{32}H_{54}O_2$ | 81·7 | 11·5 |
| Hexanoate | 81·9 | 11·5 | $C_{33}H_{56}O_2$ | 81·8 | 11·6 |
| Heptanoate | 81·9 | 11·5 | $C_{34}H_{58}O_2$ | 81·9 | 11·65 |
| Octanoate | 82·1 | 11·7 | $C_{35}H_{60}O_2$ | 82·0 | 11·7 |
| Nonanoate | 82·0 | 11·7 | $C_{36}H_{62}O_2$ | 82·1 | 11·75 |
| Decanoate | 82·3 | 11·9 | $C_{37}H_{64}O_2$ | 82·2 | 11·85 |
| Laurate | 82·4 | 12·0 | $C_{39}H_{68}O_2$ | 82·4 | 12·0 |
| Myristate | 82·6 | 12·2 | $C_{41}H_{72}O_2$ | 82·55 | 12·1 |
| Palmitate | 82·65 | 12·2 | $C_{43}H_{76}O_2$ | 82·7 | 12·2 |
| Stearate | 82·9 | 12·3 | $C_{45}H_{80}O_2$ | 82·8 | 12·3 |

was poured into water (50 ml.) and extracted with ether, and the extract washed with 2N-sulphuric acid until the dimethylaniline had been removed. Washing was continued with water, aqueous sodium hydrogen carbonate, and water, the ether solution dried ($Na_2SO_4$), and the solvent removed. The residual esters were crystallised from glacial acetic acid and ethanol until the transition temperatures were constant.

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THE UNIVERSITY, HULL. [*Received, April 25th,* 1956.]

## 727. *A Search for New Trypanocides. Part III.* Some Analogues of Suramin.*

By A. ADAMS, J. N. ASHLEY, and H. BADER.

Some symmetrical ureas are described, which are based on the structure of Suramin but contain thiazol-2-yl, 2-pyridyl, 5-sulpho-2-pyridyl, and 4-carboxy-3-hydroxyphenyl groups, instead of the naphthalenetrisulphonic acid grouping. All the compounds were inactive against *Trypanosoma congolense* and *T. rhodesiense* infections in mice.

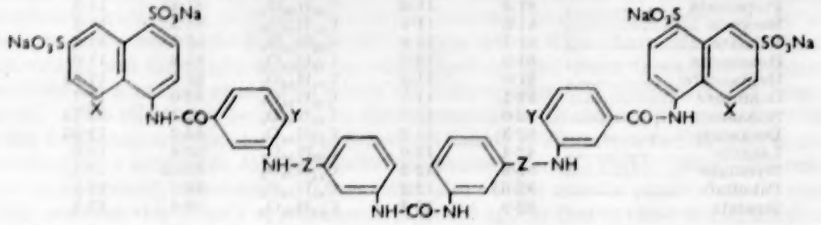
SURAMIN has been used for many years in the treatment of the early stages of human trypanosomiasis, and since the structure of this drug was established as (I) by Fourneau [1] and his collaborators many analogous ureas have been prepared. None of these had any appreciable trypanocidal activity (cf., *inter alia*, Fourneau *et al.*[1] and Fischl and Schlossberger [2]), and it was concluded that any deviation, however slight, from the structure (I) reduced the activity very considerably or gave an inactive compound.

Since analogues prepared by other workers were based on naphthalene substituted by various sulphonic acid residues, it was decided, when the present work was started some years ago, to make a more drastic change, and synthesise ureas of type (VIII), based on heterocyclic systems. Wills and Wormall [3] recently examined the enzyme-inhibiting capacity of Suramin and various analogues of it. One of these was the related sulphonamide (II). Spinks [4] also studied a series of compounds including the product (III), which was stated to have only a trace of trypanocidal activity. Pratesi and Raffa [5] also prepared analogues such as the symmetrical ureas derived from 1-[*p*-(*p*-aminobenzenesulphonamido)benzenesulphonamido]naphthalene-6-sulphonic acid and 1-(*m*-aminobenzenesulphonamido)naphthalene-3 : 6 : 8-trisulphonic acid, in which all the amido-groups of the Suramin type of

* Part II, *J.*, 1956, 3293.

[1] Fourneau, Trefouel, Trefouel, and Vallée, *Compt. rend.*, 1924, **178**, 675; *Ann. Inst. Pasteur*, 1924, **38**, 81.
[2] Fischl and Schlossberger, "Handbook of Chemotherapy," Roebuck & Son, Baltimore, 1933.
[3] Wills and Wormall, *Biochem. J.*, 1950, **47**, 158.
[4] Spinks, *ibid.*, 1948, **42**, 109.
[5] Pratesi and Raffa, *Farmaco. sci. e tec.* (*Pavia*), 1946, **1**, 21; *Chem. Abs.*, 1946, **40**, 4360.

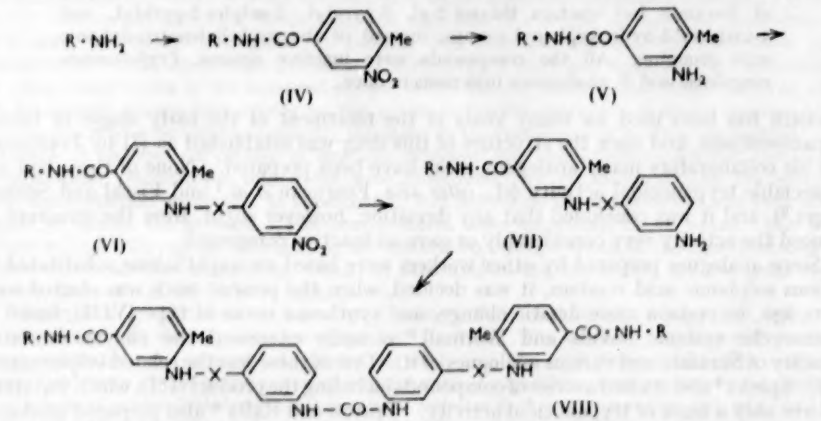
compound were replaced by sulphonamido-linkages. Although no information regarding trypanocidal activity of these products was given, we thought it of interest to include some ureas containing sulphonamido-linkages amongst those prepared by us.



(I): X = $SO_3Na$, Y = Me, Z = CO. (II): X = $SO_3Na$, Y = H, Z = $SO_2$

(III): X = OH, Y = Me, Z = $SO_2$

The terminal groups R of the ureas (VIII) prepared were thiazol-2-yl, 2-pyridyl, 5-sulpho-2-pyridyl, and 4-carboxy-3-hydroxyphenyl. Condensations of the amines $R{\cdot}NH_2$ and (V) with substituted benzoyl chlorides were easily performed in dry pyridine, in preference to use of the Schotten–Baumann conditions (cf. previous authors), and very good yields (75—95%) of the amides (IV) and (VI) were obtained. This method failed only in the case of 4-aminosalicylic acid from which unidentifiable low-melting products were obtained. Attempted condensation of this acid with 4-methyl-3-nitrobenzoyl chloride under Schotten–Baumann conditions gave *ON*-di-(4-methyl-3-nitrobenzoyl)-*m*-aminophenol, the salt derived from 4-aminosalicylic acid, and 4-methyl-3-nitrobenzoic acid. The desired amide (IVg) was finally prepared in good yield by boiling the reactants in acetone. This compound, together with others in the series, was unusual in that it did not decompose, or dissolve in, saturated aqueous sodium hydrogen carbonate. However, boiling aqueous



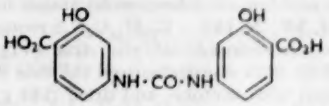
(IV) (V) (VI) (VII) (VIII)

a, X = CO, R = thiazol-2-yl.
b, X = $SO_2$, R = ,,
c, X = CO, R = 2-pyridyl.
d, X = $SO_2$, R = ,,
e, X = CO, R = 5-sulpho-2-pyridyl.
f, X = $SO_2$, R = ,,
g, X = CO, R = 4-carboxy-3-hydroxyphenyl.

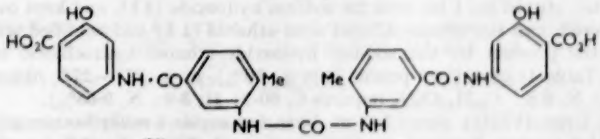
sodium carbonate gave a sodium salt, insoluble in cold and only slightly soluble in boiling water.

Reduction of the nitro-amides had previously been carried out by iron in acetic acid. In the present work the nitro-amides (IV) and (VI) were reduced catalytically in solution or suspension in a convenient solvent, with Adams platinum catalyst. In some cases the

choice of solvents was important. Thus reductions of the nitro-compounds (IVa and c) could be performed in acetic acid, but gave mixtures when attempted in ethanol, whilst that of (VIb) proceeded smoothly in aqueous sodium hydroxide at 20 atmospheres but only to a limited extent in acetic acid and not at all in ethanol. On the other hand, reduction of the compound (VIc) was successful in ethanol, whereas no solid product could be isolated when acetic acid was used. Compounds containing sulphonic or carboxylic acid groups were reduced in solution or suspension in aqueous sodium hydroxide, at room temperature and 20 atmospheres.




(IX)




(X)

The amines (VIIa, c, and d) which did not contain free acidic substituents reacted with carbonyl chloride in aqueous acetic acid, in presence of sodium acetate. These reactions were usually carried out at room temperature, but in the case of (VIId) a temperature of 90° was necessary. Those amines containing carboxy- or sulpho-substituents (VIIe, f, and g), and (VIIb) which was insoluble in aqueous acetic acid, were treated with carbonyl chloride in aqueous sodium hydroxide at room temperature, to give the ureas (VIIIe, f, g, and b) in good yield. Higher yields were obtained when carbonyl chloride was introduced slowly, and the reaction temperature was kept at 0°, thus avoiding any fission of the amide linkages in the alkaline medium. This method was also used to prepare the symmetrical ureas (IX) and (X) from 4-aminosalicylic acid and *p*-(3-amino-4-methylbenzamido)salicylic acid (Vg).

All the ureas were inactive against *T. congolense* and *T. rhodesiense* infections in mice.

## Experimental

*2-(4-Methyl-3-nitrobenzamido)thiazole* (IVa).—4-Methyl-3-nitrobenzoyl chloride (21 g.) was slowly added with stirring and cooling to 2-aminothiazole (10·5 g.) dissolved in dry pyridine (30 c.c.) and cooled to 0°, after which the mixture was heated on the steam-bath for 10 min. The solid mass was added to water (1 l.), and the finely divided product was filtered off, washed with water, and dried (24·3 g., 88%). Recrystallisation from ethanol gave *2-(4-methyl-3-nitrobenzamido)thiazole*, colourless hexagonal plates, m. p. 192° (Found: C, 50·2; H, 3·6; N, 15·8. $C_{11}H_9O_3N_3S$ requires C, 50·2; H, 3·4; N, 16·0%).

*4-(4-Methyl-3-nitrobenzamido)salicylic Acid* (IVg).—4-Aminosalicylic acid (153 g., 1 mol.) and 4-methyl-3-nitrobenzoyl chloride (100 g., 0·5 mol.) in acetone (1 l.) were boiled under reflux for 1 hr. The solid product was filtered off and stirred for 10 min. with a solution of anhydrous sodium carbonate (110 g.) in water (1500 c.c.) to remove excess of aminosalicylic acid. The residual sodium salt was washed with water and stirred with N-hydrochloric acid (1500 c.c.). Recrystallisation of the resulting solid from pyridine gave *4-(4-methyl-3-nitrobenzamido)salicylic acid* (146 g., 92%) as short white needles, m. p. 264—265° (decomp.) [Found: C, 57·0; H, 3·9; N, 8·9; $CO_2$, lost on decomp. at m. p., 14·0%; equiv. (by titration), 319. $C_{15}H_{12}O_6N_2$ requires C, 57·0; H, 3·8; N, 8·9; $CO_2$, 13·9%; equiv., 316·4]. The acid gave a violet colour with aqueous ferric chloride, but did not affect saturated aqueous sodium hydrogen carbonate, though it was slightly soluble in hot 2N-sodium carbonate from which the sodium salt crystallised in fine needles, m. p. >300°.

*2-(3-Amino-4-methylbenzamido)thiazole* (Va).—A suspension of the nitro-amide (IVa) (105·2 g.) in acetic acid (2 l.) was hydrogenated at room temperature and atmospheric pressure

in the presence of Adams catalyst (5 g.). Hydrogenation required 20 hr. during which grey crystals separated. These were dissolved by warming and the catalyst was then filtered off. After addition of an equal volume of water and basification with aqueous sodium hydroxide, the precipitate (76·8 g., 82%) was filtered off; recrystallisation from ethanol gave 2-(3-*amino*-4-*methylbenzamido*)*thiazole* in fine, colourless needles, m. p. 208° (Found: C, 56·8; H, 4·8; N, 17·9. $C_{11}H_{11}ON_3S$ requires C, 56·65; H, 4·7; N, 18·0%).

2-(4-*Methyl*-3-m-*nitrobenzamidobenzamido*)*thiazole* (VIa).—This was prepared similarly to the simpler analogue (IVa) from *m*-nitrobenzoyl chloride and 2-(3-amino-4-methylbenzamido)-thiazole (Va) in pyridine. Recrystallisation of the product (46·9 g., 94%) from aqueous pyridine gave 2-(4-*methyl*-3-m-*nitrobenzamidobenzamido*)*thiazole* in fine, colourless needles, m. p. 283—285° (Found: C, 56·9; H, 3·9; N, 14·7. $C_{18}H_{14}O_4N_4S$ requires C, 56·5; H, 3·7; N, 14·7%).

4-(4-*Methyl*-3-m-*nitrobenzamidobenzamido*)*salicylic Acid* (VIg).—The amine (Vg) (143 g.) was heated under reflux for 3 hr. with *m*-nitrobenzoyl chloride (93 g.) and acetone (2 l.). The product was filtered off, washed with acetone, and dried (183 g.). It was stirred for 10 min. with a solution of sodium hydrogen carbonate (100 g.) in water (3 l.); the solid was filtered off, washed with water, stirred for 1 hr. with 2N-sodium hydroxide (4 l.), and kept overnight. The mixture was filtered, and the filtrate diluted with ethanol (1 l.) and acidified with acetic acid. Purification of the product by the sodium hydroxide–ethanol–hydrochloric acid treatment (see footnote *d*, Table 1) gave fawn prisms (108 g., 50%), m. p. 271—272° (decomp.) (Found: C, 60·5; H, 4·1; N, 9·8. $C_{22}H_{17}O_7N_5$ requires C, 60·7; H, 3·9; N, 9·65%).

*Symmetrical Urea* (VIIIa) *from* 2-(3-m-*Aminobenzamido*-4-*methylbenzamido*)*thiazole*.—The amine (VIIa) (11·6 g.) was dissolved in warm acetic acid (200 c.c.). After cooling, a solution of sodium acetate trihydrate (11·6 g.) in water (11·6 c.c.) was added, and a slow stream of carbonyl chloride was passed into the mixture. An exothermic reaction occurred, and after 30 min. the mixture was poured into water (1·5 l.) and kept overnight. The product, which was gelatinous, darkened during attempted drying at 100°; the remainder of the urea was therefore dissolved in boiling pyridine (500 c.c.). The solution was treated with charcoal, filtered, and poured into cold water (3 l.), and the milky precipitate coagulated by warming on the steam-bath. The product was then filtered off, washed with water, and dried at 100°. Recrystallisation from aqueous pyridine or aqueous acetic acid gave the *product* (6·8 g., 56%) in short, colourless needles, m. p. 305—307° (Found: C, 56·2; H, 5·0; N, 14·0; loss at 115°/vac., 7·6. $C_{37}H_{30}O_5N_8S_2,3H_2O$ requires C, 56·6; H, 4·6; N, 14·3; $H_2O$, 7·0%).

2-(4-*Methyl*-3-m-*nitrobenzensulphonamidobenzamido*)*thiazole* (VIb).—*m*-Nitrobenzene-sulphonyl chloride (28·5 g.) was added to a solution of 2-(3-amino-4-methylbenzamido)thiazole (Va) (30 g.) in pyridine (155 c.c.) which was then heated on the steam-bath for 1 hr. The solution was poured, with stirring, into water (5 l.) and kept overnight, by which time the sticky precipitate had solidified. Recrystallisation of the solid from aqueous pyridine gave 2-(4-*methyl*-3-m-*nitrobenzenesulphonamidobenzamido*)*thiazole*, straw-coloured needles, m. p. 215—217° (Found: C, 48·5; H, 3·3; N, 13·3. $C_{17}H_{14}O_5N_4S_2$ requires C, 48·8; H, 3·3; N, 13·4%).

The other *ureas* and *intermediates* were prepared by methods similar to those recorded above and are recorded in Tables 1—3.

*Salt of* 4-*Aminosalicylic Acid with* 4-*Methyl*-3-*nitrobenzoic Acid.—Method I.* 4-Methyl-3-nitrobenzoyl chloride (15·5 g.) was added to 4-aminosalicylic acid (11·9 g.) in 3% aqueous sodium hydroxide (200 c.c.), and the mixture was shaken for 1 hr. The solid was filtered off, washed with water, and dried. It was stirred for 10 min. with N-sodium hydroxide (50 c.c.), and the

TABLE 1. *Nitroamides* (IV) *and amino-amides* (V).

| Subst. | | Yield (%) | M. p. | Formula | Found (%) C | H | N | Required (%) C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|
| *Nitro-amides* | | | | | | | | | | |
| IVc | Plates [a] | 96 | 152—153° | $C_{12}H_{11}O_3N_3$ | 60·9 | 4·3 | 16·6 | 60·7 | 4·3 | 16·3 |
| IVe | Needles [a] | 78 | 316 [b] | $C_{18}H_{11}O_6N_3S$ | 46·6 | 3·6 | 12·55 | 46·25 | 3·3 | 12·5 |
| *Amino-amides* | | | | | | | | | | |
| Vc | Rectangular prisms [f] | 64 | 182·5—183 | $C_{12}H_{13}ON_3$ | 68·6 | 6·2 | 18·65 | 68·7 | 5·7 | 18·5 |
| Ve | Needles [a] | 70 [b] | 306 | $C_{18}H_{13}O_4N_3S$ [c] | 48·3 | 4·6 | 13·15 | 48·7 | 4·2 | 13·1 |
| Vg | Fawn prisms [d] | 91 | 251 [a] | $C_{18}H_{14}O_5N_4$ | 62·8 | 5·0 | 9·8 | 62·9 | 4·9 | 9·8 |

[a] With decomp. [b] Pptd. by acid from solution in dil. NaOH. [c] Reduction carried out in dil. NaOH at 25°/20 atm. [d] $+H_2O$ (Loss at 100°/vac., 4·5. Required: $H_2O$, 4·2%). [e] Pptd. by acid from solution in dil. NaOH–EtOH. [f] From EtOH or $C_6H_6$. [g] From EtOH.

TABLE 2. *Nitro-amides* (VI) *and amino-amides* (VII).

| Subst. | X | | Yield (%) | M. p. | Formula | Found (%) C | H | N | Required (%) C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Nitro-amides* | | | | | | | | | | | |
| VIc | CO | Needles [a] | 90 | 228·5° | $C_{20}H_{16}O_4N_4$ | 63·8 | 4·35 | 14·75 | 63·8 | 4·25 | 14·9 |
| VId | $SO_2$ | Pale yellow prisms [b] | 90 | 192—193 | $C_{19}H_{16}O_5N_4S$ | 55·5 | 4·1 | 13·6 | 55·3 | 3·9 | 13·6 |
| VIe | CO | Colourless [c] | 74 | 312 | $C_{20}H_{16}O_7N_4S$ | 52·9 | 4·0 | — | 52·6 | 3·5 | — |
| VIf | $SO_2$ | Plates [c] | 44 | 223 | $C_{19}H_{16}O_9N_4S_2,H_2O$ | 44·9 | 3·7 | 10·5 | 44·7 | 3·5 | 10·95 |
| *Amino-amides* | | | | | | | | | | | |
| VIIa | CO | Needles [d] | 90 [e] | 270—270·5 | $C_{18}H_{16}O_3N_4S$ | 61·4 | 4·7 | 15·7 | 61·4 | 4·55 | 15·9 |
| VIIb | $SO_2$ | Fawn prisms [f] | 94 [g] | 287—289 | $C_{17}H_{16}O_5N_4S_2$ | 52·8 | 4·2 | 14·6 | 52·6 | 4·1 | 14·4 |
| VIIc | CO | Needles [h] | 90 [i] | 217 | $C_{20}H_{18}O_2N_4$ | 69·4 | 5·3 | 16·0 | 69·4 | 5·2 | 16·2 |
| VIId | $SO_2$ | ,, | 80 [i] | 206—207 | $C_{19}H_{18}O_3N_4S$ [j] | 59·5 | 4·8 | 14·45 | 59·7 | 4·7 | 14·7 |
| VIIe | CO | Cream-coloured [c] | 74 [k] | 287 [c] | $C_{20}H_{18}O_5N_4S,H_2O$ | 53·8 | 4·8 | 12·6 | 54·05 | 4·5 | 12·6 |
| VIIf | $SO_2$ | Colourless [c] | 83 [g] | 240—250 [c] | $C_{19}H_{18}O_6N_4S_2,H_2O$ [l] | 47·5 | 4·8 | 11·55 | 47·5 | 4·2 | 11·7 |
| VIIg | CO | Fawn prisms [l] | 50 | 243—244 [c] | $C_{22}H_{19}O_5N_3$ | 64·7 | 4·8 | 10·1 | 65·2 | 4·7 | 10·4 |

[a] With decomp. [b] Pptd. by acid from solution in dil. NaOH–EtOH. [c] Reduction in acetic acid at 68°/20 atm. [d] Reduction in dil. NaOH at 25°/21 atm. [e] Reduction in EtOH. [f] Found: S, 8·5. Required: S, 8·4%. [g] Reduction in suspension in dil. NaOH. [h] Found: S, 13·5. Required: S, 13·3%. [i] Loss at 110°/vac., 3·6. Required: $H_2O$, 3·8%. [j] From MeOH or dil. pyridine. [k] From dil. pyridine. [l] From EtOH. [m] From pyridine.

TABLE 3. *Ureas* (VIII).

| Subst. | | Yield (%) | M. p. | Formula | Found (%) C | H | N | Required (%) C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|
| VIIIb | Pale yellow prisms [a] | 70 | 240—245° [a] | $C_{35}H_{30}O_7N_8S_1,H_2O$ [b] | 51·4 | 4·0 | 13·6 | 51·2 | 3·9 | 13·7 |
| VIIIc | Needles [c] | 53 | 266 | $C_{41}H_{34}O_8N_8,0·5H_2O$ [d] | 67·8 | 4·9 | 15·45 | 67·7 | 4·8 | 15·4 |
| VIIId | Cream-coloured [e] | 60 | 220 [a] | $C_{39}H_{34}O_7N_8S_2,4H_2O$ [d] | 54·2 | 4·8 | 12·9 | 54·3 | 4·9 | 13·0 |
| VIIIe | " | 91 | 300 [a] | $C_{41}H_{34}O_{11}N_8S_2,4H_2O$ [b] | 52·3 | 4·8 | 11·55 | 51·8 | 4·4 | 11·8 |
| VIIIf | " | 84 | [f] | $C_{39}H_{34}O_{13}N_8S_4,3H_2O$ [b] | 46·1 | 4·3 | 10·8 | 46·6 | 4·0 | 11·15 |
| VIIIg | Pale brown | 65 | 250—253 [a] | $C_{45}H_{34}O_{11}N_6,2H_2O$ [g] | 61·7 | 4·6 | 9·5 | 61·8 | 4·6 | 9·6 |

[a] With decomp. [b] Pptd. by acid from solution in dil. NaOH–EtOH. [c] Loss at 112°/vac., 2·05. Required: $H_2O$, 2·2%. [d] Loss at 115°/vac., 7·6. Required: $H_2O$, 7·0%. [e] Pptd. from EtOH by ether. [f] Found: S, 7·6. Required: S, 7·4%. [g] Found: S, 6·65. Required: S, 6·7%. [h] Slowly darkens above 295°. [i] Loss at 112°/vac., 5·0. Required: $H_2O$, 5·4%. [j] Loss at 112°/vac., 4·6. Required: $H_2O$, 4·1%. [k] From dil. pyridine.

mixture was filtered. Addition of acetic acid to the filtrate gave 4-methyl-3-nitrobenzoic acid (2·9 g.), m. p. 190°. The residue left after stirring with aqueous sodium hydroxide was washed with water and dried (5·9 g., m. p. 178—183°). Recrystallisation from toluene gave *ON-di-(4-methyl-3-nitrobenzoyl)-m-aminophenol*, white needles, m. p. 167—168°, then resolidifies, and remelts at 191°. The product gave no colour with aqueous ferric chloride; neither did it couple with β-naphthol after attempted diazotisation, or decompose aqueous sodium carbonate. The compound did not depress the m. p. of a specimen prepared from 4-methyl-3-nitrobenzoyl chloride and *m*-aminophenol by the Schotten–Baumann method (Found: C, 60·7; H, 4·0; N, 9·7. $C_{22}H_{17}O_7N_3$ requires C, 60·7; H, 3·9; N, 9·65%).

The filtrate from the original reaction was acidified with acetic acid and afforded a solid which after crystallisation from toluene gave the *salt* (7·7 g.) of 4-aminosalicylic acid and 4-methyl-3-nitrobenzoic acid as pale yellow prisms, m. p. and mixed m. p. with an authentic specimen (method II), 165° (decomp.) [Found: C, 54·5; H, 4·4; N, 8·2%; equiv., 168·5 (by titration). $C_7H_7O_3N,C_8H_7O_4N$ requires C, 53·9; H, 4·2; N, 8·4%; equiv., 167·1]. The product was acid to litmus, and liberated carbon dioxide from saturated aqueous sodium hydrogen carbonate. It gave a violet colour with aqueous ferric chloride and a red colour after diazotisation and coupling with β-naphthol.

*Method II.* Sodium 4-aminosalicylate (2·11 g.) in water (10 c.c.) was added to 4-methyl-3-nitrobenzoic acid (1·81 g.) in N-sodium hydroxide (10 c.c.). The clear yellow mixture was

acidified with acetic acid, and the cream-coloured precipitate was recrystallised from toluene to give the salt (3·2 g.), pale yellow prisms, m. p. 165° (decomp.).

*Symmetrical Urea* (IX) *from 4-Aminosalicylic Acid.*—Sodium 4-aminosalicylate dihydrate (10 g.), dissolved in a mixture of 2N-sodium hydroxide and acetone (1 : 1; 100 c.c.), was treated with carbonyl chloride as described above. The *product*, purified by the sodium hydroxide–ethanol–hydrochloric acid treatment, formed white crystals (83%), m. p. 300° (Found: C, 53·0; H, 3·6; N, 8·3; loss at 112°/vac., 2·3. $C_{15}H_{12}O_7N_2,0{\cdot}5H_2O$ requires C, 52·8; H, 3·8; N, 8·2; $H_2O$, 2·6%).

*Symmetrical Urea* (X) *from 4-(3-Amino-4-methylbenzamido)salicylic Acid.*—This *urea* was prepared (80%) similarly and crystallised from pyridine in white needles, m. p. 289—290° (decomp.) (Found: C, 62·2; H, 4·6; N, 9·3. $C_{31}H_{26}O_9N_4$ requires C, 62·2; H, 4·4; N, 9·4%).

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Dagenham, Essex.

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## 728. *The Constitution of a Xylan from Norway Spruce* (Picea excelsa).

By G. O. Aspinall and (Miss) Mary E. Carter.

Fractionation of Norway spruce hemicellulose yielded two xylan-rich components. One of these was converted into a fully methylated xylan, hydrolysis of which yielded 2 : 3 : 4-tri-*O*-methyl-, 2 : 3-di-*O*-methyl-, and 3-*O*-methyl-D-xylose, and 3-*O*-methyl-2-*O*-(2 : 3 : 4-tri-*O*-methyl-D-glucuronosyl)-D-xylose in the approximate molar ratio of 1 : 69 : 8 : 21. It is concluded from these and other experiments that this xylan has a straight chain of 80—85 1 : 4-linked β-D-xylopyranose residues with every fifth residue carrying a terminal 4-*O*-methyl-D-glucuronic acid residue linked through position 2.

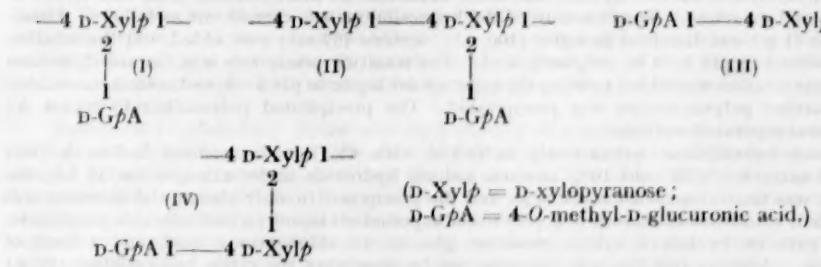
Recent investigations [1] have indicated that the xylans from land plants all contain backbones of 1 : 4-linked β-D-xylopyranose residues, but that the various xylans differ considerably in the nature, number, and mode of linkage of other sugar residues attached as side-chains. For example, beechwood xylan [2] contains side-chains of single 4-*O*-methyl-D-glucuronic acid residues linked to $C_{(2)}$ of xylose, whereas the xylans from esparto grass and the cereal straws are often characterised by the presence of L-arabofuranose residues linked to xylose through $C_{(3)}$, although in some cases D-glucuronic acid residues are also found. It was of interest, therefore, to extend investigations to the xylans from the coniferous woods or gymnosperms. The isolation of xylobiose and the aldobiouronic acid, 2-*O*-(4-*O*-methyl-D-glucuronosyl)-D-xylose, from the partial acid hydrolysis of black spruce (*Picea nigra*) and Scots pine (*Pinus sylvestris*) [3] suggested that xylans of the type found in beechwood might also be present in these woods. On the other hand, arabinose has been found in the hydrolysates from coniferous woods,[4] and no evidence was available as to whether this sugar was a constituent of a xylose-containing polysaccharide. This paper describes the structure of a xylan isolated from Norway spruce wood (*Picea excelsa*).

The spruce hemicellulose was isolated by extraction of the delignified sawdust with cold aqueous sodium hydroxide; previous experiments had shown that only small yields of alkali-soluble polysaccharides could be obtained by direct extraction of the wood without removal of lignin with chlorous acid. The crude hemicellulose yielded a complex mixture of sugars on hydrolysis, but by careful precipitation from aqueous solution and by

[1] Hirst, *J.*, 1955, 2974.
[2] Aspinall, Hirst, and Mahomed, *J.*, 1954, 1734.
[3] Gorrod and Jones, *J.*, 1954, 2522.
[4] Gustafsson, Pettersson, and Lindh, *Paperi ja Puu*, 1951, **33**, 300.

precipitation of contaminating polysaccharides as the copper complex two xylan-rich fractions were isolated. Both of these fractions gave, on hydrolysis, acidic oligosaccharides, reduction of whose methyl ester methyl glycosides with potassium borohydride, followed by hydrolysis, yielded 4-*O*-methyl-D-glucose and xylose. As 4-*O*-methyl-D-glucose was not detected on hydrolysis of the xylan fractions, it is clear that this sugar was formed by the reduction of 4-*O*-methyl-D-glucuronic acid, a fairly common constituent of plant polysaccharides.

One of the xylan fractions was converted into its fully methylated derivative, during which process the contaminating polysaccharides containing sugar residues other than xylose and glucuronic acid were lost. Hydrolysis of the methylated xylan gave 2 : 3 : 4-tri-*O*-methyl-, 2 : 3-di-*O*-methyl-, and 3-*O*-methyl-D-xylose, together with a mixture of acidic components. The acidic fraction had equivalent weight 378 (Calc. for a glucuronosylxylose tetramethyl ether, 382), but chromatography indicated the presence of at least two components, one of which travelled on the chromatogram at the same rate as 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid. The major component of the acidic fraction was identified as 3-*O*-methyl-2-*O*-(2 : 3 : 4-tri-*O*-methyl-D-glucuronosyl)-D-xylose in the following way. Reduction of the derived methyl ester methyl glycoside with lithium aluminium hydride followed by hydrolysis gave 2 : 3 : 4-tri-*O*-methylglucose and 3-*O*-methylxylose, together with a small amount of 2 : 3-di-*O*-methylxylose. A portion of the reduced acidic fraction was remethylated and after hydrolysis yielded two main components, 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose and 3 : 4-di-*O*-methyl-D-xylose, with traces of 2 : 3 : 4-tri-*O*-methyl- and 3-*O*-methyl-xylose, and 2 : 3 : 4-tri-*O*-methylglucose; no 2 : 3-di-*O*-methylxylose could be detected. It follows from these observations that the 4-*O*-methyl-D-glucuronic acid residues are attached directly to the backbone of D-xylose residues through position 2 as in (I). The chromatographic identification of 2 : 3-di-*O*-methylxylose on hydrolysis of the reduced acidic fraction, and of 2 : 3 : 4-tri-*O*-methyl- and 3-*O*-methyl-xylose on hydrolysis after further methylation suggests that the acidic fraction also contained a trisaccharide derived from the xylan as in (II). The absence of 2 : 3-di-*O*-methylxylose on hydrolysis after remethylation excludes the possibility that the backbone of 1 : 4-linked xylose units might be terminated by a glucuronic acid unit as in (III) or that the side-chains might consist of disaccharide units as in (IV).




The hydrolysis products from the methylated xylan, namely, 2 : 3 : 4-tri-*O*-methyl-, 2 : 3-di-*O*-methyl-, and 3-*O*-methyl-D-xylose, and the acidic fraction (calculated as tetra-*O*-methylaldobiouronic acid) were isolated in the approximate molar ratio of 1 : 69 : 8 : 21. A molecular-weight determination by the isothermal-distillation method (by the courtesy of Dr. C. T. Greenwood and Mr. W. N. Broatch) gave a value of 17,000 ± 500 (degree of polymerisation, 101 ± 3) for the methylated xylan. This value, taken together with the value of one non-reducing xylose end-group per *ca.* 100 sugar residues, indicates that the backbone of xylose residues is unbranched. It is concluded, therefore, that this xylan has a straight chain of 80–85 1 : 4-linked β-D-xylopyranose residues, with, on the average, every fifth residue carrying a terminal 4-*O*-methyl-D-glucuronic acid residue linked through $C_{(2)}$. This xylan is probably only one of many closely related molecular species present in the wood, and it is of interest that no arabinose residues were found. It is possible,

therefore, that the arabinose residues present in Norway sprucewood may occur in association with galactose residues, as is the case in the ε-galactan from European [5] and North American [6] larches, and in the arabogalactan from Jeffery pine.[7] However, on present evidence the presence, in spruce, of araboxylans, of the type found in the cereal straws, cannot be excluded.

These results indicate that this Norway spruce xylan resembles closely the hemicellulose A from beechwood,[2] although differing slightly in chain length and in the proportion of 4-*O*-methyl-D-glucuronic acid residues linked as side-chains. Although no detailed structural studies have been carried out on the xylose-containing polysaccharides from aspen,[8] black spruce, and Scots pine [3] woods, it will be recalled that evidence for the presence of xylans of the same general type has been obtained by the isolation of xylobiose and the aldobiouronic acid, 2-*O*-(4-*O*-methyl-D-glucuronosyl)-D-xylose, on partial acid hydrolysis of these woods. Whilst the xylans from different plants [1] exhibit considerable variations in detailed molecular structure, our present knowledge suggests that the xylans from both deciduous and coniferous woods contain the same structural features and differ only in chain length and/or number of uronic acid residues attached as side-chains. However, further investigations of other wood xylans will be necessary before such a generalisation could be regarded as established.

## Experimental

Paper chromatography was carried out on Whatman No. 1 filter paper, with the upper layers of the following solvent systems (v/v): (A) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3); (B) butan-1-ol–ethanol–water (5 : 1 : 4); (C) butan-1-ol–formic acid–water (500 : 115 : 385). Paper ionophoresis was carried out [9] in borate buffer at pH 10. Optical rotations were observed at room temperature (16—18°).

*Extraction and Fractionation of Spruce Hemicellulose.*—Extractive-free sawdust was delignified by Wise, Murphy, and D'Addieco's [10] method. In a typical extraction spruce holocellulose (40 g.) was treated with cold 4% aqueous sodium hydroxide under nitrogen for 18 hr. The filtrate was acidified with acetic acid to pH 4 and the crude hemicellulose (3 g.) was precipitated by the addition of two volumes of acetone. Chromatographic examination of the hydrolysate showed xylose, arabinose, mannose, an aldobiouronic acid, and traces of glucose and galactose. Fractionation of the hemicellulose was carried out as follows: Hemicellulose (1 g.) was dissolved in water (100 ml.), acetone (67 ml.) was added, and the solution was acidified to pH 3—4 by sulphuric acid. The resulting precipitate was discarded, sodium carbonate solution was added to bring the supernatant liquor to pH 5—6, and acetone was added until further polysaccharide was precipitated. The precipitated polysaccharide (xylan A; 0·2 g.) was separated and dried.

Spruce holocellulose, exhaustively extracted with 4% aqueous sodium hydroxide, was further extracted with cold 10% aqueous sodium hydroxide under nitrogen for 18 hr., the extract was neutralised with acetic acid, and the precipitate (mainly glucan and mannan) was discarded. Addition of acetone (0·5 vol.) to the supernatant liquor yielded a further precipitate, which gave on hydrolysis xylose, mannose, glucose, an aldobiouronic acid, and a trace of galactose. A xylan-rich fraction was obtained by dissolving the crude hemicellulose (12 g.) in 4% sodium hydroxide solution (1 l.) and adding to the solution glycerol (3 ml.) followed by 0·5M-copper sulphate solution. The pale blue precipitate, which was first formed, was removed at the centrifuge and the addition of copper sulphate was stopped before the dark blue gelatinous precipitate of the xylan complex appeared. The unprecipitated polysaccharide was recovered by neutralisation of the solution with acetic acid followed by precipitation with acetone (*ca.* 0·5 vol.). This procedure was repeated four times until the addition of copper sulphate no longer resulted in the formation of a pale blue precipitate. The polysaccharide (xylan B; 3 g.)

[5] Campbell, Hirst, and Jones, *J.*, 1948, 774; Jones, *J.*, 1953, 1672; Aspinall, Hirst, and Ramstad, unpublished results.
[6] White, *J. Amer. Chem. Soc.*, 1941, **63**, 2871; 1942, **64**, 302, 1507, 2838.
[7] Wadman, Anderson, and Hassid, *ibid.*, 1954, **76**, 4097.
[8] Jones and Wise, *J.*, 1952, 3389.
[9] Consden and Stainer, *Nature*, 1952, **169**, 783.
[10] Wise, Murphy, and D'Addieco, *Paper Trade J.*, 1946, **122**, 35.

isolated from these fractionations gave on hydrolysis xylose and an aldobiouronic acid, together with smaller amounts of mannose, glucose, and galactose.

*Examination of Xylan-rich Fractions.*—Xylan A had $[\alpha]_D$ −38° (*c*, 0·39 in N-sodium hydroxide) [Found: uronic anhydride (by decarboxylation), 15·0; OMe, 2·7%] and chromatographic examination of the hydrolysate showed the presence of xylose (58%), arabinose (17%), and glucose + galactose (8%). Xylan B had $[\alpha]_D$ −44° (*c*, 0·32 in N-sodium hydroxide) (Found: uronic anhydride, 18·9; OMe, 1·8%) and chromatographic examination of the hydrolysate showed the presence of xylose (63%), mannose (13%), and glucose + galactose (7%).

Xylan A (3 g.) was hydrolysed with N-sulphuric acid (50 ml.) at 100° for 4 hr. The hydrolysate was neutralised with barium carbonate, and barium ions were removed with Amberlite resin IR-120. The resulting solution was poured on to a column of charcoal–Celite, and the monosaccharides were eluted with water. Elution with ethyl methyl ketone–water (1 : 19) yielded a fraction containing aldobiouronic acid, which was converted into the methyl ester methyl glycoside and treated with a solution of potassium borohydride (300 mg.) in water (20 ml.) for 24 hr. Excess of borohydride was destroyed by the addition of acetic acid, and the solution was de-ionised by successive treatments with Amberlite resins IR-120 and IR-4B. The resulting syrup was hydrolysed with 0·8N-hydrochloric acid (15 ml.) for 6 hr. at 100°. Chromatographic examination of the hydrolysate showed the presence of 4-*O*-methylglucose and xylose. The fastest-moving component (56 mg.) was separated on filter sheets, with solvent A, but attempts to characterise the sugar by conversion into the crystalline 4-*O*-methyl-D-glucosazone failed. However, an impure fraction, shown by circular paper chromatography [11] to contain mainly the desired compound, gave an *X*-ray powder photograph with the same lines as those from an authentic sample.

Xylan B (300 mg.) was hydrolysed with N-sulphuric acid (10 ml.) at 100° for 10 hr. The hydrolysate was neutralised with barium carbonate, de-ionised with Amberlite resin IR-120, and concentrated to a syrup. The acidic component (23 mg.) was separated on filter sheets with solvent A, and was converted into the methyl ester methyl glycoside, which was treated with a solution of potassium borohydride (15 mg.) in water (5 ml.) for 24 hr. After destruction of the excess of borohydride with acetic acid, 2N-hydrochloric acid (5 ml.) was added, and the solution was heated at 100° for 6 hr. After neutralisation and de-ionisation, chromatographic examination of the hydrolysate showed the presence of 4-*O*-methylglucose, xylose, and a trace of glucose.

*Methylation of Xylan.*—Xylan B (10 g.) was methylated fifteen times with methyl sulphate and sodium hydroxide. The partially methylated polysaccharide, suspended in acetone–water (1 : 1), was stirred with Amberlite resin IR-120 to remove sodium ions, the solution was taken to dryness, and the polysaccharide (4·7 g.) was precipitated from chloroform solution by the addition of light petroleum (b. p. 60—80°). Methylation of the product with methyl iodide and silver oxide gave methylated spruce xylan (4·0 g.) {OMe, 40·3%; $[\alpha]_D$ −43·7° (*c*, 0·25 in $CHCl_3$)}.

*Hydrolysis of Methylated Xylan and Separation of Methylated Sugars.*—Methylated xylan (3·0 g.) was dissolved in 2N-hydrochloric acid (230 ml.) and kept at room temperature for 17 days. After addition of water (230 ml.), the solution was heated at 100° for 4 hr. and kept at room temperature for 20 hr. This procedure was repeated three times (constant rotation), and a small quantity of insoluble material (*ca.* 0·1 g.) was separated and hydrolysed by successive treatments with boiling methanolic hydrogen chloride and with N-hydrochloric acid at 100°. The combined hydrolysates were neutralised with silver carbonate, the acidic components were converted into barium salts by treatment with barium carbonate, and the solution was concentrated to a syrup (2·9 g.).

The methylated sugars (2·9 g.) were fractionated on cellulose [11] (74 × 3·8 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3; later, 1 : 1) saturated with water, and butan-1-ol partly saturated with water as eluants, to give five fractions, and a further fraction was obtained by elution of the cellulose with water. Apart from fraction 1 (23 mg.), all other fractions were contaminated with acidic components. Fractions 2 (88 mg.), 4 (0·212 g.), and 6 (0·564 g.) contained only acidic substances and were combined. Portions of fractions 3 (1·510 g.) and 5 (0·188 g.) were each separated on filter sheets with solvent B, and the proportions of acidic and neutral components were determined. The results showed that the following methylated sugars were present in the hydrolysate: tri-*O*-methylxylose [0·023 g., 1·03% (mol.)], di-*O*-methylxylose (1·435 g., 69·2%), mono-*O*-methylxylose (0·161 g., 8·4%), and methylated aldobiouronic acid [0·949 g., 21·3% (calc. as tetramethylaldobiouronic acid)].

[11] Hough, Jones, and Wadman, *J.*, 1949, 2511.

*Examination of Neutral Sugars.*—Fraction **1** crystallised and had m. p. and mixed m. p. (with **2 : 3 : 4**-tri-*O*-methyl-D-xylose) **88—91°** (Found : OMe, **48·0**. Calc. for $C_8H_{16}O_5$ : OMe, **48·4%**). The neutral component from fraction **3** (Found : OMe, **34·6**. Calc. for $C_7H_{14}O_5$ : OMe, **34·8%**) was identified as **2 : 3**-di-*O*-methyl-D-xylose by conversion into the aniline derivative, m. p. and mixed m. p. **122°**, and into **2 : 3**-di-*O*-methyl-D-xylonamide, m. p. and mixed m. p. **132°**. The neutral component from fraction **5** (Found : OMe, **17·9**. Calc. for $C_6H_{12}O_5$ : OMe, **18·9%**) travelled on the chromatogram at the same rate as 2- and/or 3-*O*-methyl-D-xylose, but ionophoretic examination showed the presence of the 3-methyl ether with only traces of the 2-methyl ether.

*Examination of the Acidic Fraction.*—Chromatographic examination in solvent C of the acidic fractions showed that they all contained two components, one travelling at the same rate as **2 : 3 : 4**-tri-*O*-methyl-D-glucuronic acid. The combined acidic fractions had equiv. **378** (calc. for a tetra-*O*-methylaldobiouronic acid, $C_{15}H_{26}O_{11}$, **382**).

The acid (**200** mg.) was refluxed with methanolic **1%** hydrogen chloride (**40** ml.) for **6** hr. The product, after neutralisation, was dissolved in dry ether (**65** ml.), lithium aluminium hydride (**300** mg.) was added, and the solution was refluxed for **6** hr. Excess of hydride was destroyed by water, and the solution was acidified with sulphuric acid and extracted with chloroform (**6** × **50** ml.). The extract was evaporated to a syrup, which was hydrolysed by hot **0·8N**-hydrochloric acid for **6** hr. After neutralisation with silver carbonate, part of the hydrolysate was separated on filter sheets with solvent B, to give fractions *a* (**61** mg.) and *b* (**16** mg.). Fraction *a* contained two components, chromatographically and ionophoretically indistinguishable from **2 : 3 : 4**-tri-*O*-methyl-D-glucose (major) and **2 : 3**-di-*O*-methyl-D-xylose (minor) severally; the major component was further separated and on demethylation gave only glucose (Found : OMe, **40·0**. Calc. for $C_6H_{12}O_6$ : OMe, **41·9%**). Fraction *b* travelled on the chromatogram at the same rate as 2- and/or 3-*O*-methyl-D-xylose, but at a different rate from the 4-methyl ether. Ionophoretic examination showed that only the 3-methyl ether was present.

The acid (**375** mg.) was refluxed with methanolic **1%** hydrogen chloride (**60** ml.) for **6** hr. After neutralisation with silver carbonate and removal of solvent, the methyl ester methyl glycoside was reduced with lithium aluminium hydride (**300** mg.) in boiling methylal (**70** ml.) for **2** hr. Excess of hydride was destroyed by water, the methylal layer was separated, and the aqueous layer was extracted with chloroform and ether. The aqueous layer was acidified with dilute sulphuric acid, the sulphate and aluminium ions were removed as precipitates on addition of barium hydroxide, and the barium and lithium ions were removed as the insoluble carbonates. The resulting solution was taken to dryness and combined with the organic extracts to give a syrup (**241** mg.). The reduced aldobiouronic acid was remethylated with methyl iodide and silver oxide, and the methylated disaccharide (**259** mg.) was hydrolysed with **0·8N**-hydrochloric acid (**20** ml.) at **100°** for **6** hr. and after neutralisation gave a syrup (**208** mg.). Chromatographic examination of the hydrolysate showed two main conponents, tetra-*O*-methylglucose and **3 : 4**-di-*O*-methylxylose, together with traces of **2 : 3 : 4**-tri-*O*-methyl- and 3-*O*-methyl-xylose, and **2 : 3 : 4**-tri-*O*-methylglucose; no **2 : 3**-di-*O*-methylxylose could be detected. The main components were separated on filter sheets with solvent B, to yield **2 : 3 : 4 : 6**-tetra-*O*-methyl-D-glucose, m. p. [after recrystallisation from light petroleum (b. p. **40—60°**) containing a little ether] and mixed m. p. **95·5—96·5°**, and **3 : 4**-di-*O*-methyl-D-xylose, identified by conversion into **3 : 4**-di-*O*-methyl-D-xylonolactone, m. p. and mixed m. p. **64—66°**.

The authors thank Professor E. L. Hirst, F.R.S., for his interest and advice, Messrs. Alex. Cowan and Sons Ltd. for financial assistance (to M. E. C.), and the Rockefeller Foundation for a grant.

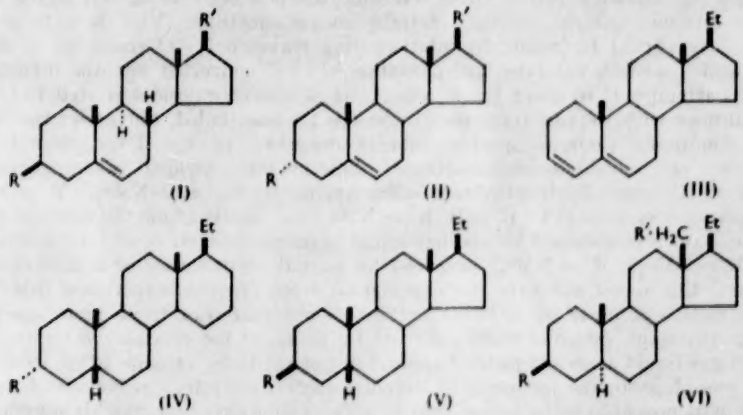
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, May 17th,* 1956.]

## 729. *The Constitution of Conessine. Part IX.* Further Studies with Steroidal Amines related to Conessine.*

By R. D. Haworth, L. H. C. Lunts, and J. McKenna.

The base, m. p. 130°, previously [1] obtained by treatment of pregn-5-en-3β-yl toluene-*p*-sulphonate with dimethylamine has been identified as 3α-dimethylaminopregn-5-ene by its properties and reactions including Hofmann degradation to pregna-3 : 5-diene, and by identification of its dihydro-derivative as 3α-dimethylaminopregnane; the results † demonstrate that virtually complete inversion of configuration at $C_{(3)}$ occurs during the replacement reaction with the unsaturated toluene-*p*-sulphonate, in opposition to Shoppee's earlier generalisation.[2] The synthesis is reported of 3β-dimethylaminopregn-5-ene, a conessine degradation product, and some Emde reductions of other conessine derivatives and related amines are described.

Haworth, McKenna, and Powell [1] found that the reaction of dimethylamine with pregn-5-en-3β-yl toluene-*p*-sulphonate (I; R = *p*-Me·$C_6H_4$·$SO_3$, R′ = Et) failed to yield the then expected 3β-dimethylaminopregn-5-ene (I; R = $NMe_2$, R′ = Et), an amine previously [4] isolated by degradation of conessine; an isomeric amine, m. p. 130°, which furnished a dihydro-derivative, m. p. 78—79°, was instead obtained in the replacement reaction. Parallel reactions [1] with cholest-5-en-3β-yl toluene-*p*-sulphonate (I; *p*-Me·$C_6H_4$·$SO_3$, R′ = $C_8H_{17}$) were subsequently found,[5,6] unexpectedly,‡ to yield




3α-amines (II; R = $NH_2$, NHMe, $NMe_2$, R′ = $C_8H_{17}$), and the data now presented indicate that the base, m. p. 130°, is 3α-dimethylaminopregn-5-ene (II; R = $NMe_2$, R′ = Et). Thus the infrared absorption spectrum (max. at 797, 826, and 1667 cm.$^{-1}$; the corresponding cholestene base has bands [6] at 796, 827, and 1660 cm.$^{-1}$) and optical rotation ("Δ value" [7] of the unsaturated amine relative to 3α-dimethylaminopregnane is −247°)

* Part VIII, *J.*, 1955, 986.

† This work was essentially complete in March, 1954, when Professor C. W. Shoppee, F.R.S., was informed of our views on the structure of the dimethylaminopregnene. The unsaturated base was subsequently synthesised by Shoppee and his collaborators.[3]

‡ Cf. ref. 3.

[1] Haworth, McKenna, and Powell, *J.*, 1953, 1110.
[2] Pierce, Richards, Shoppee, Stephenson, and Summers, *J.*, 1955, 694.
[3] Shoppee, *J.*, 1946, 1147.
[4] Haworth, McKenna, and Whitfield, *J.*, 1953, 1102.
[5] Šorm, Lábler, and Černý, *Chem. Listy*, 1953, **47**, 418; 1954, **48**, 1058.
[6] Haworth, Lunts, and McKenna, *J.*, 1955, 986.
[7] Barton and Klyne, *Chem. and Ind.*, 1948, 755.

support this structure. Hofmann degradation of the base yielded pregna-3 : 5-diene (III), which we synthesised for comparison by reaction of pregn-5-en-3β-yl toluene-*p*-sulphonate (I; R = *p*-Me·$C_6H_4$·$SO_3$, R′ = Et) with boiling dimethylaniline.[8] Finally, the dihydro-derivative, m. p. 78—79°, of the unsaturated amine was identified as 3α-dimethylamino-pregnane (IV; R = $NMe_2$) by synthesis of this base from pregnan-3-one, obtained in our work by catalytic hydrogenation under alkaline conditions of pregn-4-en-3-one.[9] Reduction of the ketoxime with sodium and pentyl alcohol gave a mixture of 3α(equatorial; main component)- and 3β(axial)-aminopregnanes (IV and V; R = $NH_2$); methylation of this mixture yielded 3α- and 3β-dimethylaminopregnane (IV and V; R = $NMe_2$). The latter base was identical with the product, m. p. 124°, obtained by Shoppee and his co-workers [2] by treatment of pregnan-3α-yl toluene-*p*-sulphonate (IV; R = *p*-Me·$C_6H_4$·$SO_3$) with dimethylamine, and the yield in our reaction sequence is very low owing to the axial conformation of the corresponding primary amine; Shoppee and his co-workers [2] did not isolate any 3β-amine on reduction of pregnan-3-one oxime with sodium and ethyl alcohol.

3β-Dimethylaminopregn-5-ene (I; R = $NMe_2$, R′ = Et) has been prepared in the following manner. Ammonolysis of pregn-5-en-3β-yl toluene-*p*-sulphonate yielded a mixture of amines from which, after experience with the related cholesterylamines, the primary 3β-epimer was isolated by precipitation with digitonin. After decomposition of the digitonin complex in the usual manner, methylation of the primary base yielded 3β-dimethylaminopregn-5-ene, identical with the conessine degradation product.[4]

3β-Dimethylamino*allo*pregnane (VI; R = $NMe_2$, R′ = H), previously obtained by a lengthy degradation sequence [4] from conessine, has now been prepared from the alkaloid by the following simple process. Tetrahydroconessimethine (VI; R = R′ = $NMe_2$), obtained by partial Hofmann degradation (ring fission only) of conessine or dihydro-conessine followed by catalytic hydrogenation,[4,10] was converted into the dimethiodide. Previous attempts [11] to effect Emde reductions of dimethochlorides related to conessine by treatment with sodium amalgam in aqueous medium failed, but under the modified Emde conditions (sodium–liquid ammonia) described in the Experimental section reduction of tetrahydroconessimethine dimethiodide yielded *allo*pregnane (VI; R = R′ = H) and 3β-dimethylamino*allo*pregnane (VI; R = $NMe_2$, R′ = H). No hexahydro*apo*conessine (VI; R = H, R′ = $NMe_2$) was isolated from the reaction mixture, but this base was obtained by sodium–liquid ammonia reduction of a monomethiodide (VI; R = $NMe_3I$, R′ = $NMe_2$) prepared by partial methylation of tetrahydroconessi-methine; this result supports the expectation from previous experience that the 3β-dimethylamino-group in the reduced methine should quaternise much more rapidly than the dimethylamino-group originally derived by fission of the conessine heterocyclic ring. The sodium–liquid ammonia method appears in general to be superior to the conventional Emde procedure for the reduction of steroidal quaternary salts: reduction of the meth-iodides of monoacid bases such as hexahydro*apo*conessine gave better yields of hydrocarbon than those previously recorded.[12]

## Experimental

*Hofmann Degradation of 3α-Dimethylaminopregn-5-ene.*—3α-Dimethylaminopregn-5-ene [1] (21 mg.) was converted into dimethiodide and thence into an aqueous solution of dimetho-hydroxide in the usual way; the solution was concentrated and the residue pyrolysed at 140° (bath)/0·005 mm. Crystallisation of the product from acetone gave pregna-3 : 5-diene (6 mg.), m. p. 84°, undepressed on admixture with a specimen prepared as described below.

*Pregna-3 : 5-diene.*—Pregna-5-en-3β-yl toluene-*p*-sulphonate (89 mg.) in dry dimethyl-aniline (1 c.c.) was heated under reflux for 20 min., and the neutral *product* (50 mg.) isolated with ether in the usual way and recrystallised from acetone; it then had m. p. 87—88°, $[\alpha]_D$

[8] Cf. ref. 4.
[9] Cf. Wilds, Johnson, and Sutton, *J. Amer. Chem. Soc.*, 1950, **72**, 5524.
[10] Favre, Haworth, McKenna, Powell, and Whitfield, *J.*, 1953, 1115.
[11] Haworth, McKenna, Powell, and Woodward, *J.*, 1951, 1736.
[12] Haworth, McKenna, and Whitfield, *J.*, 1949, 3127.

$-138°$ (*c* 0·52 in $CHCl_3$), $\lambda_{max.}$ 2280, 2350, 2435 Å (ε 19,600, 20,600, 13,500 respectively) (Found: C, 88·8; H, 11·2. $C_{21}H_{33}$ requires C, 88·7; H, 11·3%).

*Pregnan-3-one.*—Pregn-4-en-3-one (242 mg.) in 0·5% alcoholic potassium hydroxide (10 c.c.) was hydrogenated (uptake at N.T.P., 19·4 c.c. Calc. for one double bond, 18·1 c.c.) in presence of 15% palladised charcoal (100 mg.); the product had m. p. (from acetone) 114° (lit.,[13] 115°). The oxime crystallised from ethanol in colourless rods, m. p. 161—162° (Found: N, 4·5. Calc. for $C_{21}H_{35}ON$: N, 4·4%). Pierce *et al.*[2] give m. p. 165—167°.

*3α- and 3β-Dimethylaminopregnane.*—Pregnan-3-one (128 mg.) in dry technical pentyl alcohol (20 c.c.) was treated at reflux temperature with sodium (2·5 g.) added portionwise during 1·25 hr., and the basic product was isolated as mixed hydrochlorides (92 mg.), m. p. 320—322°. The basic mixture was methylated with formaldehyde and formic acid, and the tertiary bases were again isolated as a mixture of hydrochlorides (103 mg.) which was fractionally crystallised from acetone, yielding needles (7 mg.), m. p. 290—294° (decomp.), and needles (48 mg.), m. p. 239—241° (decomp.). The amine from the first hydrochloride, on crystallisation from acetone, had m. p. 132° undepressed on admixture with an authentic but lower-melting (m. p. 124°) sample of 3β-dimethylaminopregnane kindly supplied by Professor C. W. Shoppee, F.R.S. The lower-melting hydrochloride yielded a base which crystallised from acetone in plates, m. p. 77—78°, undepressed on admixture with a sample of 3α-dimethylaminopregnane prepared by reduction of 3α-dimethylaminopregn-5-ene [1] (Found: N, 4·4. Calc. for $C_{23}H_{41}N$: N, 4·2%).

*Separation of 3β- from 3α-Aminocholest-5-ene with Digitonin.*—A mixture of 3α-*iso*propylideneaminocholest-5-ene [6] (10 mg.) and the 3β-epimer (13 mg.) was hydrolysed with hydrochloric acid, and the mixture of primary bases in 95% ethanol (5 c.c.) was treated with digitonin (5 c.c. of 1% solution in 95% ethanol). After 42 hr. the insoluble digitonide (24 mg.) was collected and decomposed with pyridine–ether in the usual manner. Methylation of the basic product from this decomposition yielded 3β-dimethylaminocholest-5-ene, m. p. and mixed m. p. 146—147° (4 mg.).

*Synthesis of 3β-Dimethylaminopregn-5-ene.*—Pregn-5-en-3β-yl toluene-*p*-sulphonate (355 mg.) was heated with excess of liquid ammonia at 95° for 9·5 hr., and the hydrochlorides of steroidal basic products separated into fractions (96 and 32 mg.) respectively soluble and insoluble in ether. Recrystallisation of the soluble fraction from acetone yielded fine needles, m. p. 264—265°, $[\alpha]_D$ +18° (*c* 0·7 in $CHCl_3$) (Found: Cl, 10·2. $C_{21}H_{36}NCl$ requires Cl, 10·5%), presumably [14] *6β-amino-3*: 5-cyclo*pregnane hydrochloride*. The ether-insoluble hydrochloride fraction was basified and the product treated with digitonin in the manner described above for the aminocholestenes; the insoluble digitonide (20 mg.) was then decomposed and the resultant amine methylated with formaldehyde and formic acid. Crystallisation of the product from acetone gave 3β-dimethylaminopregn-5-ene, needles, m. p. 115°, not depressed on admixture with a sample, m. p. 117°, prepared [6] from conessine.

*Emde Reduction of Tetrahydroconessimethine Dimethiodide.*—The *dimethiodide*, needles (from ether–methanol), m. p. 307—308° (decomp.) (Found: N, 4·6; I, 39·4, 37·9. $C_{25}H_{46}N_2.2CH_3I$ requires N, 4·3; I, 38·6%), was prepared by heating the methine with excess of methyl iodide at 100° for 49 hr. This salt (375 mg.) in liquid ammonia (100 c.c.) was treated portionwise with sodium until a permanent blue colour developed. After 8 hr. the ammonia was allowed to evaporate and neutral and basic fractions were isolated. Crystallisation of the neutral fraction from ether–methanol yielded *allo*pregnane (18 mg.) as needles, m. p. and mixed m. p. 80°. The basic product, which yielded a hydrochloride insoluble in water, crystallised from acetone in needles (135 mg.), m. p. 95—96° undepressed on admixture with an authentic specimen of 3β-dimethylamino*allo*pregnane of the same m. p. No hexahydro*apo*conessine could be isolated from the basic fraction from the reduction by either chromatography or selective quaternisation with methyl iodide (hexahydro*apo*conessine quaternises very much more slowly than 3β-dimethylamino*allo*pregnane).

*Reduction of Tetrahydroconessimethine Monomethiodide.*—Tetrahydroconessimethine (215 mg.) and methyl iodide (1 c.c.) were heated under reflux in methanol (10 c.c.) for 3 hr. *Tetrahydroconessimethine monomethiodide*, precipitated with ether and recrystallised from ether–methanol, was obtained as needles (203 mg.), m. p. 297° (decomp.) (Found: I, 24·0. $C_{25}H_{46}N_2.CH_3I$ requires I, 24·6%). Reduction of this salt as before yielded hexahydro*apo*conessine (7 mg.), m. p. and mixed m. p. 63—64°, and tetrahydroconessimethine (88 mg.), m. p. 80—81° after recrystallisation from acetone.

[13] Marker and Lawson, *J. Amer. Chem. Soc.*, 1938, **60**, 2438.
[14] Cf. Julian, Magnani, Meyer, and Cole, *J. Amer. Chem. Soc.*, 1948, **70**, 1834.

***Reduction of Hexahydroapoconessine Methiodide.***—The conversion of hexahydro*apo*-conessine (158 mg.) into methiodide by refluxing in methanol (10 c.c.) with methyl iodide (1 c.c.) was only 34% complete in 4 hr., and more prolonged heating (>12 hr.) was required for reasonable yields by this method. Reduction of the methiodide (204 mg.) in the manner described above yielded *allo*pregnane (15 mg.), m. p. 83—84°, and hexahydro*apo*conessine (125 mg.), m. p. 64—65°.

We thank the Department of Scientific and Industrial Research for a maintenance allowance (to L. H. C. L.) and Imperial Chemical Industries Limited for a grant towards the expenses of the investigation.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, May 31st,* 1956.]

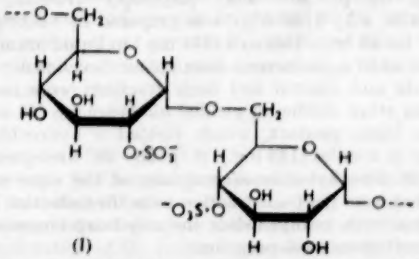
## 730. *The Distribution of Ester Groups in Dextran Sulphate and their Stability towards Hydrolytic Reagents.*

By C. R. RICKETTS.

Dextran sulphate having, on average, one sulphate group per glucose unit, was oxidised with sodium metaperiodate. Formic acid (0·2 mol.) was produced, indicating the presence of glucose units without sulphate groups in the molecule. Alkaline hydrolysis removed sulphate groups from dextran sulphate and was slower the higher the degree of sulphation. By ionophoresis in borate buffer, sugars with $M_0$ values corresponding to glucose, gulose, altrose, and mannose were found in the hydrolysate. Acidic hydrolysis of dextran sulphate rapidly removed sulphate groups without formation of new hexoses.

DEXTRAN SULPHATE is prepared by the action of chlorosulphonic acid in pyridine on the dextran produced by *L. mesenteroides*. Preparations have been made w th widely differing mean molecular weights, from the esters of oligosaccharides (*M ca.* $10^3$) through the intermediate ranges to esters of native dextran (*M ca.* $10^6$), and with varying degrees of sulphation almost up to the theoretical maximum. A blood-anticoagulant drug has been developed using dextran sulphate of low molecular weight,[1] and some novel procedures for the separation of plasma proteins have been developed which use preparations of high molecular weight.[2] Little is known about the distribution of sulphate groups in the dextran sulphate molecule and their stability toward hydrolytic reagents.

To simplify discussion of the distrubtion of sulphate groups in the dextran sulphate molecule, consider the case of an unbranched dextran having an average of one sulphate group per glucose unit. In a uniform distribution each unit would carry a sulphate group.



(I)

A departure from the uniform distribution would result in some glucose units having more than one sulphate group while others had none. On oxidation with sodium metaperiodate, only those glucose units having no sulphate group have the three adjacent hydroxyl groups necessary to yield formic acid. In the experiments described an unbranched dextran having, on average, 1·08 sulphate groups per glucose unit yielded 0·20 mol. of formic acid per glucose sulphate unit with the consumption of 0·43 mol. of sodium metaperiodate.

[1] Ricketts and Walton, *Chem. and Ind.*, 1952, 869; British Pharmacopœia Addendum, 1955, p. 16.
[2] Walton and Oncley, *J. Amer. Chem. Soc.*, in the press.

These results indicate the presence of glucose units without sulphate groups in the dextran sulphate molecule.

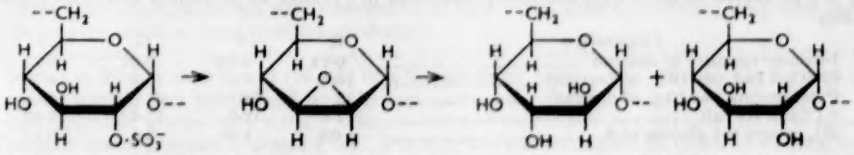
Percival,[3] discussing the stability of carbohydrate sulphates under alkaline conditions, pointed out that a sulphate group is susceptible to hydrolysis only if there is an adjacent hydroxyl group in the *trans*-position so that an ethylene oxide type of anhydro-ring is readily formed. A well-defined example is due to Duff [4] who converted 1 : 6-anhydro-β-D-galactopyranose 2-sulphate into 1 : 6-2 : 3-dianhydro-β-D-talopyranose by treatment with sodium methoxide. The analogy between sulphuric esters and the much studied toluene-*p*-sulphonic esters of sugars is evident. Dextran sulphate (I; $SO_3^-$ at arbitary positions) presents a favourable case for examining the application of these reactions to polysaccharides because, with the exception of terminal glucose units, the reducing groups are blocked, there are no sulphates of primary alcohol groups and adjacent hydroxyl groups are always in the *trans*-position.

Hydrolysis of dextran sulphate is conveniently followed by means of the metachromatic reaction with the dye toluidine-blue,[5] which forms a purple salt with anions of high molecular weight, one molecule of dye combining with each sulphate group in dextran sulphate.[6] When shaken with light petroleum the purple salt separates at the interface,[7] leaving an aqueous solution from which dye has been removed stoicheiometrically. A colorimetric measurement thus enables the ester sulphate groups of dextran sulphate to be estimated.

Samples of three dextran sulphates, containing severally 0·17, 1·08, and 2·1 sulphate groups (average) per glucose unit, were submitted to alkaline hydrolysis. The quantity of dextran sulphate was varied so that the same amount of ester sulphate was available for hydrolysis in each experiment. Loss of sulphate groups was followed colorimetrically. The figure shows that the lower the degree of sulphation the more rapidly were ester sulphate groups removed by hydrolysis. It appears that at the higher degrees of sulphation hydrolysis is limited by the availability of free hydroxyl groups adjacent to sulphate groups.

From these considerations it seemed likely that the product obtained by alkaline hydrolysis of dextran sulphate would contain hexoses other than glucose. Dextran sulphate containing 1·08 sulphate groups per glucose unit was therefore submitted to alkaline hydrolysis under conditions which had been found to remove about half of the ester sulphate groups. After removal of sodium ions by means of an exchange resin the polymeric product was submitted to acidic hydrolysis under conditions known to hydrolyse dextran completely. The neutralised hydrolysate was submitted to paper chromatography. Though no clear resolution could be obtained there was an indication of the presence of more than one component. Ionophoresis in borate buffer on paper, followed by spraying with aniline hydrogen phthalate or silver nitrate in acetone, revealed four components: that migrating most rapidly had an $M_G$ value corresponding with glucose and it seemed likely that the other components were also hexoses.

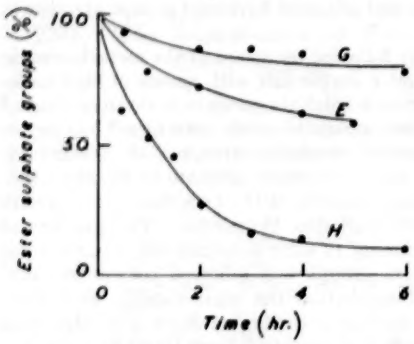
The principles, (1) formation of an ethylene oxide ring with Walden inversion at the carbon atom losing an ester group and (2) opening of the ring in two possible ways with Walden inversion at the carbon atom receiving a hydroxyl group, indicate that the hexoses formed during the alkaline and subsequent acid hydrolysis of dextran sulphate should be gulose and altrose. For example, a glucose unit of the dextran molecule having a 2-sulphate group on the pyranose ring could, on alkaline hydrolysis, give rise to the altrose configuration (see annexed scheme). Ionophoresis with control mixtures showed that two



[3] Percival, *Quart. Rev.*, 1949, **3**, 369.
[4] Duff, *J.*, 1949, 1597.
[5] Michaelis, *J. phys. Chem.*, 1950, **54**, 1.
[6] Ricketts and Walton, *Brit. J. Exp. Path.*, 1954, **35** 227.
[7] MacIntosh, *Biochem. J.*, 1941, **35**, 776.

of the components in the hydrolysate migrated with $M_G$ values corresponding to gulose and altrose. The fourth and slowest component had an $M_G$ value corresponding with that of mannose; no satisfactory explanation of this is available: in a control experiment with dextran no mannose was detected. There was no sign of hexose sulphates, probably because the sulphate groups were split off in the subsequent acid hydrolysis yielding the corresponding hexoses (see below).

Thus alkaline hydrolysis of dextran sulphate generates four of the eight isomeric hexoses in the D-series. The optimum yield of hexoses other than glucose would be expected from a dextran sulphate having an average of one sulphate group per glucose unit. Actually other hexoses were not detectable in hydrolysates of dextran sulphates having 2·1 and 0·17 sulphate groups per glucose unit. In the former case the extent of alkaline




*Showing hydrolysis of ester groups from three preparations of dextran sulphate by 2·5N-sodium hydroxide at 100°. Preparation G has 2·1, E 1·08, and H 0·17 ester sulphate groups per glucose unit.*

hydrolysis is small (see Figure). In the latter there is a preponderance of unsulphated glucose units.

By contrast with alkaline hydrolysis, acidic hydrolysis of ester sulphate groups occurs readily. From a dextran sulphate of high molecular weight (*ca.* $10^6$) containing 2·1 ester sulphate groups per glucose unit, 98% of the ester sulphate groups were removed by 0·1N-sulphuric acid at 100° in 30 minutes. The product appeared to be a partially hydrolysed dextran. This was confirmed by completing the hydrolysis and demonstrating by ionophoresis that only one hexose, corresponding in $M_G$ value with glucose, was present.

To provide a direct comparison with alkaline hydrolysis, the dextran sulphate containing 1·08 sulphate groups per glucose unit, was completely hydrolysed in acid solution and yielded only one hexose (corresponding in $M_G$ to glucose).

The four preparations of dextran sulphate were selected for their suitability for the experiments described. All unbranched dextran sulphates are composed of a selection of the nine possible types of sulphated glucose unit and therefore it is to be expected that the reactions described will apply in varying degrees to all samples of dextran sulphate.

## Experimental

*Sulphation of Dextran.*—Four preparations of sodium dextran sulphate were made by treating dry powdered dextran with chlorosulphonic acid in pyridine as previously described [8] (see Table).

| Preparation | E | F | G | H |
|---|---|---|---|---|
| Intrinsic viscosity of dextran | 0·14 | 0·03 | 0·67 | 0·32 |
| $ClSO_3H$ (ml. per 10 g. of dextran) | 16·6 | 7·0 | 15·0 | 4·7 |
| Pyridine (ml. per 10 g. of dextran) | 133 | 74 | 61 | 74 |
| S (%) in Na salt | 12·6 | 12·0 | 17·6 | 2·87 |
| $SO_4$ groups per glucose unit | 1·08 | 1·00 | 2·1 | 0·17 |

*Oxidation of Dextran Sulphate with Metaperiodate.*—Sodium dextran sulphate (E) (170·5 mg.) which had been freeze-dried and dried to constant weight *in vacuo* ($P_2O_5$ at 100°) was oxidised

[8] Ricketts, *Biochem. J.*, 1952, **55**, 129.

in 0·0342M-sodium metaperiodate (100 ml.). The formic acid produced [9] and the metaperiodate consumed [10] were determined at intervals. The results were calculated as mols. of formic acid produced and metaperiodate consumed per glucose sulphate unit :

| Time (hr.) | 48 | 72 | 96 | Mean of 72 and 96 hr. |
|---|---|---|---|---|
| $H{\cdot}CO_2H$ (mol.) | 0·195 | 0·199 | 0·203 | 0·201 |
| $IO_4^-$ consumed (mol.) | 0·427 | 0·428 | 0·434 | 0·431 |

*Alkaline Hydrolysis of Dextran Sulphate.*—The three dextran sulphates (H 40 mg.; E 10·1 mg.; G 7·2 mg.; *i.e.*, containing the same amount of ester sulphate) were dissolved in 2·5N-sodium hydroxide (20 ml.). Portions (2 ml.) were heated in sealed ampoules in a boiling-water bath. At intervals ampoules were withdrawn, cooled, neutralised, diluted, and analysed for ester sulphate.[7] A calibration curve was constructed, with preparation E as standard, and results were calculated as percentage loss of ester sulphate groups (see Figure).

*Identification of Products of Alkaline Hydrolysis.*—Dextran sulphate E (100 mg.) was heated in 2·5N-sodium hydroxide (1 ml.) as above for 5 hr. After cooling, the solution was diluted and passed through a column (70 × 10 mm. diameter) of cation-exchange resin (Zeokarb 215), then concentrated under reduced pressure to 1 ml., mixed with 2N-sulphuric acid (1 ml.), and heated in a sealed ampoule in a boiling-water bath for 5 hr. After cooling the solution was neutralised with barium carbonate. Barium salts were separated on the centrifuge and washed with water. The solution and washings were combined and concentrated under reduced pressure to 1 ml. Partition chromatography on Whatman No. 1 paper with butanol–ethanol–water (5 : 1 : 4 by vol.) at 37° showed, after spraying with aniline hydrogen phthalate and baking at 110°, only one spot whose $R_F$ value corresponded with that of glucose. Similarly with butanol–pyridine–water (6 : 4 : 3 by vol.), at room temperature only one spot ($R_F$ = that of glucose control) was detected but elongation of the spot suggested the presence of more than one component. Ionophoresis [11] in borate buffer of pH 10, followed by spraying with aniline hydrogen phthalate,[12] or silver nitrate in acetone (2·5 ml. of saturated aqueous silver nitrate in 500 ml. of acetone), revealed 4 components. Mixtures of glucose with gulose, with altrose, and with mannose were submitted to ionophoresis alongside the hydrolysate. A control spot of 2 : 3 : 4 : 6-tetra-*O*-methyl glucose enabled a correction for endosmotic flow to be applied in the calculation of $M_G$ values, which were tabulated. In the hydrolysate the mannose and gulose spots were similar and less intense than the glucose spot; the altrose spot was faint.

| | $M_G$ values | | | |
|---|---|---|---|---|
| Hydrolysate | 0·716 | 0·831 | 0·916 | 0·987 |
| Gulose + glucose | — | 0·838 | — | 1·000 |
| Hydrolysate | 0·720 | 0·807 | 0·907 | 0·980 |
| Altrose + glucose | — | — | 0·920 | 1·000 |
| Hydrolysate | 0·724 | 0·836 | 0·912 | 0·990 |
| Mannose + glucose | 0·724 | — | — | 1·000 |

In a confirmatory experiment, dextran sulphate F (100 mg. in 1 ml. of 2·5N-sodium hydroxide) was submitted to alkaline and then acidic hydrolysis, as described; electrophoresis again revealed four components with $M_G$ values close to those recorded above. However, when dextran sulphate G (72 mg. in 1 ml.) and dextran sulphate H (400 mg. in 1 ml.) were submitted to the same procedure, only one component could be detected, its $M_G$ value corresponding to that of glucose.

*Acidic Hydrolysis of Dextran Sulphate.*—Portions (2 ml.) of a solution of dextran sulphate (G; 36 mg.) in 0·1N-sulphuric acid (100 ml.) were heated in sealed ampoules in a boiling-water bath. At intervals samples were analysed for ester sulphate as previously described: 98·1% of the ester sulphate groups were removed in 30 min. under these conditions; ampoules heated for longer periods showed complete hydrolysis.

*Identification of the Products of Acidic Hydrolysis.*—Dextran sulphate (G; 100 mg.) was heated in 0·1N-sulphuric acid (10 ml.) in a boiling-water bath. After 30 min. the solution was cooled quickly and neutralised with barium carbonate. Barium salts were separated in the centrifuge and washed with water. The solution and washings were combined and concentrated under reduced pressure to about 1 ml. The solution was submitted to paper chromatography

[9] Jeanes and Wilham, *J. Amer. Chem. Soc.*, 1950, **72**, 2655.
[10] Fleury and Large, *J. Pharm. Chim.*, 1933, **17**, 107, 196.
[11] Foster, *Chem. and Ind.*, 1952, 1050; *J.*, 1953, 982.
[12] Partridge, *Nature*, 1949, **164**, 443.

with butanol–pyridine–water (6 : 4 : 3 by vol.). Spraying with aniline hydrogen phthalate followed by baking at 110° revealed signs of higher saccharides near the origin but no glucose or oligosaccharides. Hydrolysis was completed by heating the solution with an equal volume of 2N-sulphuric acid in a sealed ampoule at 100° for 5 hr. After cooling, neutralisation with barium carbonate and evaporation under reduced pressure, paper chromatography, as above, showed the presence of a substance with the same $R_F$ value as glucose and no indication of saccharides. Ionophoresis in borate buffer followed by spraying with aniline hydrogen phthalate or with silver nitrate in acetone identified glucose as the only hexose detectable after acidic hydrolysis of dextran sulphate.

To provide a direct comparison of the products of alkaline hydrolysis with those of acid hydrolysis, dextran sulphate E (200 mg.) was heated in N-sulphuric acid (5 ml.) for 5 hr. After cooling, the solution was neutralised with barium carbonate. After treatment as above, ionophoresis in borate buffer on paper revealed only one component; this had an $M_G$ value corresponding with that of glucose.

The author thanks Dr. Alan Foster of the Chemistry Department, University of Birmingham, for advice on the ionophoresis of hexoses, including some unpublished $M_G$ values, and for kindly making available authentic samples of D-altrose and D-gulose received from Dr. N. K. Richtmyer.

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## 731. *Transport to the Surface of a Rotating Disc.*

By D. P. Gregory and A. C. Riddiford.

Hitherto, experimental investigations designed to check the validity of Levich's theory [1] for transport to the surface of a rotating disc have been confined to the measurement of limiting currents over a range of stirring speeds at one experimental temperature. It is shown that these published values are lower than those predicted by the theory.

The theory has been subjected to further experimental check by studying the rate of dissolution of zinc discs in aqueous iodine solutions as a function of temperature, and of the speed of rotation of the discs. The kinematic viscosity of the solution, and the coefficient of diffusion of iodine, have been measured at each temperature. The observed rate constants characterising the transport of iodine to the surface of the discs are significantly lower than those predicted by the theory. The discrepancy has been traced to an approximation made by Levich. It is shown how this approximation can be avoided, and good agreement is then found between theory and experiment, both for the zinc–iodine system and for the limiting current.

Many studies of the rates of heterogeneous reactions between solids and solutions have been reported. Very often, the observed rate is determined partly or wholly by the transport of a solute species to or from the reacting interface, and the study of these transport processes then becomes a matter of considerable theoretical and practical importance.[1]

In principle, the simplest method of determining the contribution of the transport process to the observed rate lies in the study of quiescent systems, wherein transport is purely diffusive. In practice, however, density gradients set up in the vicinity of the interface, sometimes coupled with fortuitous thermal gradients, can lead to relative motion between the solid and the fluid, with a resultant increase in the rate of transport.

One way of avoiding this difficulty is to impress a definite velocity of sufficient magnitude upon the fluid, whereby the effect of natural convection can be made entirely negligible. This method is attractive, for it permits the study of the process by simple experimental techniques over a wide range of temperatures; but the theoretical difficulties are such that, in general, transport under conditions of forced convection must be treated

[1] Bircumshaw and Riddiford, *Quart. Reviews*, 1952, **6**, 157.

by semi-empirical methods.[2] The case where transport occurs to or from a rotating disc is of special interest since an exact solution of the equations governing mass transport has been achieved.

In 1921, von Kármán [3] showed that an exact solution of the Navier–Stokes equations governing viscous flow is possible for the case of an infinite plane lamina rotating with constant angular velocity in an infinite volume of fluid about an axis perpendicular to the lamina; the exact solution was obtained by Cochran.[4] In 1942, Levich [5] used the velocity distribution so obtained to solve the corresponding mass-transport equations for the case of fluids containing not more than three ionic species. For an electrode process when the critical solute species is uncharged or, if ionic, is present in a large excess of indifferent ions, his theory leads to the following equation for the limiting current :

$$i_{\mathrm{lim}} = 0{\cdot}620zFAc_{\infty}D^{2/3}\nu^{-1/6}\omega^{1/2} \times 10^{-3}\ \mathrm{A} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $z$ is the number of electrons involved in the electrochemical reaction, $F$ is the faraday, $A$ is the apparent area of the working surface (cm.$^2$), $c_{\infty}$ is the concentration of the critical solute species in the bulk of the solution (moles/l.), $D$ is the diffusion coefficient of this solute species (cm.$^2$/sec.), $\nu$ is the kinematic viscosity of the solution (cm.$^2$/sec.), and $\omega$ is the angular velocity of the laminar electrode (rad./sec.). The corresponding unit rate constant, $k_{\mathrm{T}}$, characterising the rate of transport of a solute species to the disc is given by the relation

$$k_{\mathrm{T}} = 0{\cdot}620D^{2/3}\nu^{-1/6}\omega^{1/2}\ \mathrm{cm./sec.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The first experimental check of this important theory was made by Siver and Kabanov,[6] who studied the limiting currents for the reduction of oxygen dissolved in dilute sulphuric acid at rotating silver and at amalgamated copper disc cathodes. They showed that $i_{\mathrm{lim}}$ is proportional to $\omega^{1/2}$, and by assuming a reasonable value for the diffusion coefficient of dissolved oxygen at the experimental temperature (20° ± 1°) they reported good agreement between the observed values of $i_{\mathrm{lim}}$ and those computed from the theory. Subsequently, they investigated the discharge of hydrogen ion at a rotating amalgamated copper disc cathode from a solution $2 \times 10^{-3}$N in hydrochloric acid, which was made 0·1N in potassium chloride to suppress ionic migration.[7] Using a value for the diffusion coefficient of hydrogen ion based upon mobility data, they reported agreement between theory and experiment to within 3% at the one temperature studied (18°).

More recently, Hogge and Kraichman [8] have studied the limiting currents for the reduction of tri-iodide ion at a rotating platinum disc cathode. 0·1N-Potassium iodide was used as supporting electrolyte, and the effect of varying the angular velocity at different concentrations of tri-iodide ion was determined at 25·7°. A linear relationship was found between $i_{\mathrm{lim}}$ and $\omega^{1/2}$ for each concentration. They measured the kinematic viscosity of the solution and, from the theory, calculated the only undetermined quantity, *i.e.*, the diffusion coefficient of the tri-iodide ion. They claim that the value so obtained ($D = 1{\cdot}021 \times 10^{-5}$ cm.$^2$/sec. for the tri-iodide ion) compares favourably with those found by non-electrolytic methods, and cite a value of $D = 1{\cdot}08 \times 10^{-5}$ cm.$^2$/sec. at 25° obtained by Edgar and Diggs [9] for a solution 0·05N in iodine and 0·25N in potassium iodide. In this they are mistaken : the value actually reported by Edgar and Diggs is 1·08 cm.$^2$/day, or $1{\cdot}25 \times 10^{-5}$ cm.$^2$/sec., more than 20% higher than their value.

Finally, these authors have investigated the reduction of silver ion at a rotating silver disc cathode, a large excess of potassium nitrate being used as supporting electrolyte.[10] From their results, they have calculated the two values $D = 1{\cdot}416 \times 10^{-5}$ cm.$^2$/sec. at 25°

[2] Agar, *Discuss. Faraday Soc.*, 1947, **1**, 26.
[3] von Kármán, *Z. angew. Math. Mech.*, 1921, **1**, 244.
[4] Cochran, *Proc. Camb. Phil. Soc.*, 1934, **30**, 365.
[5] Levich, *Acta Physicochim. U.R.S.S.*, 1942, **17**, 257.
[6] Siver and Kabanov, *J. Phys. Chem., U.S.S.R.*, 1948, **22**, 53.
[7] *Idem, ibid.*, 1949, **23**, 428.
[8] Hogge and Kraichman, *J. Amer. Chem. Soc.*, 1954, **76**, 1431.
[9] Edgar and Diggs, *ibid.*, 1916, **38**, 253.
[10] Kraichman and Hogge, *J. Phys. Chem.*, 1955, **59**, 986.

and $1{\cdot}458 \times 10^{-5}$ cm.$^2$/sec. at 25·2° for silver ion at very low concentration in 0·2N-potassium nitrate solution. These values are significantly lower than the corresponding value $D = 1{\cdot}485 \times 10^{-5}$ cm.$^2$/sec. which they have computed from Onsager's limiting law for diffusion.[11]

It seemed desirable to subject Levich's theory to a more detailed experimental investigation, and since the earlier studies were all of limiting currents at one temperature, it was decided to check the validity of equation (2) over a range of temperatures by studying a reaction whereby the disc material is consumed during the process. The reaction between zinc and aqueous iodine solutions was chosen since the observed rate has been shown to be solely determined by the rate at which iodine can be transported to the zinc surface.[12] The published data for the diffusion coefficient of iodine in potassium iodide solutions are meagre,[13] so the appropriate values have been determined.

## Experimental

*Materials.*—" AnalaR " iodine, potassium iodide, sodium thiosulphate, and sulphuric acid were used without further purification. The zinc foil was of electrolytic grade (99·9%).

Fig. 1.

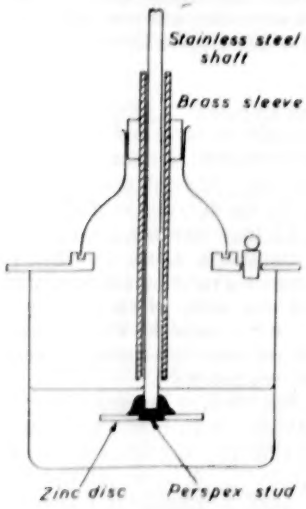
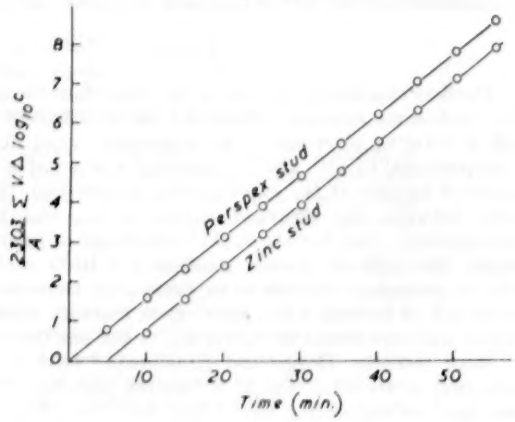



Fig. 2.




*Apparatus.*—The theory refers to an infinite plane lamina, *i.e.*, the diameter of the disc must be very much larger than the thickness of the transport boundary layer (*ca.* $10^{-3}$ cm.). Accordingly, discs 5·30 cm. in diameter were cut from zinc foil 0·5 mm. thick; later, this thickness was increased to *ca.* 3 mm. A threaded hole was cut in the centre of each disc to take a Perspex stud, which in turn was screwed to the stainless-steel stirring shaft (Fig. 1). A jig was made to ensure that each disc was cut to the same diameter, and that the thread was cut perpendicular to the plane of the disc. The end of the stud was turned flush with the lower face of the disc. The upper surface and edges of the disc were protected from attack by a thin coat of " Tufnol " lacquer, which was baked on to polymerise it. Preliminary tests, in which a disc was coated completely, showed that this lacquer was impervious to iodine solutions. These tests also served to show that the loss of iodine from the reaction vessel was negligible.

The stirring shaft was rotated at known speeds by means of a stroboscopic assembly similar to that previously described;[14] ball-races and a heavily lacquered brass sleeve (Fig. 1) ensured the absence of " whip."

[11] Onsager, *Ann. N.Y. Acad. Sci.*, 1945, **46**, 241; Gosting and Harned, *J. Amer. Chem. Soc.*, 1951, **73**, 159.
[12] Bircumshaw and Riddiford, *J.*, 1952, 701.
[13] *Idem*, *J.*, 1951, 1490.
[14] *Idem*, *J.*, 1951, 598.

The size and shape of the reaction vessel are important since the theory specifies an infinite volume of solution, *i.e.*, the rotating disc must be the only boundary surface. Preliminary runs, with discs 5·30 cm. in diameter and rotating at 146 r.p.m. in beakers of different sizes, showed that the observed rate is independent of the vessel diameter when this is greater than *ca.* 11 cm. The rate is also independent of the height of the disc above the bottom of the vessel provided that this distance is greater than *ca.* 0·5 cm. The vessel finally used was *ca.* 12·5 cm. in diameter, and was closed by a flat Perspex lid. The disc and stirring shaft could be lowered into the solution through a hole cut in the Perspex lid until a glass dome mounted on the stirring assembly located in an annular groove, so sealing the vessel (Fig. 1). The thermostat maintained the temperature constant to within $\pm 0{\cdot}05°$.

*Method.*—A solution which was 0·02N in iodine and 0·08N in potassium iodide was made approximately 0·001N in sulphuric acid to suppress the formation of a basic coating on the zinc surface;[14] 500 ml. of this solution were warmed to the thermostat temperature, degassed, and placed in the reaction vessel. The disc was cleaned with fine emery paper, washed with distilled water, and fitted to the stirring shaft. The joint between the Perspex stud and the shaft, and the exposed part of the shaft, were coated with paraffin wax. With the motor running, the disc was lowered into the solution. The joint between the dome and the groove in the Perspex lid was sealed with a little water. After some 5 min., when the motor had steadied to the required speed, a 5 ml. sample was withdrawn by pipette and titrated against 0·005N-sodium thiosulphate solution. Further samples were withdrawn at 5-min. intervals. After the run, the disc was removed from the solution, washed with distilled water, and stored under 0·001N-sulphuric acid. All the volumetric apparatus had been calibrated, and the appropriate corrections were applied. In evaluating the unit rate constant, $k_T$, allowance must be made for the decrease in volume each time a sample is removed. Bradley's method[8] was used, which avoids undue weighting of the first titration, $k_T$ being evaluated graphically by using the first-order expression: $k_T t = (2{\cdot}303 \Sigma V \Delta \log_{10} c)/A$, where $t$ is the time in min., $A$ is the *total* area of the underside of the disc and stud, and $\Delta \log_{10} c$ denotes the difference in the logarithm of the concentration at the beginning and end of an interval for which the volume is $V$. The initial volume of solution was varied over the range 400—600 ml. without effect on the observed rate constant, except for the highest speed studied (328 r.p.m.) at which a low result was obtained with 400 ml. of solution. For this reason, 500 ml. of solution were used in the later work, and the stirring speed was kept below 300 r.p.m. The results of early runs under seemingly identical conditions were of poor reproducibility. One fault was traced to the gassing of the solution, bubbles being formed on the underside of the disc: previous de-gassing of the solution eliminated this trouble. The presence of small bubbles increases the observed rate constant although the exposed area of zinc is decreased. These bubbles may promote turbulence, with a consequent increase in rate which is greater than any effect due to the blocking of part of the surface. A second fault was traced to the occasional trapping of a large bubble (*ca.* 1 cm. diam.) underneath on lowering the disc into the solution. Abnormally high results could usually be traced to a fault in the protective lacquer coating the upper, non-working surface. Experiments were performed at least in duplicate, and standard runs (25°, 146 r.p.m.) were conducted at frequent intervals as a check.

*Effect of Perspex and Zinc Centre Studs.*—The observed values of $k_T$ under the standard conditions (25°, 146 r.p.m.), and using Perspex centre studs, are shown in Table 1. The inert patch of Perspex at the centre of the working surface was *ca.* 1 cm. in diameter. Other runs were conducted with zinc centre studs, and the results are also shown in Table 1. Fig. 2 shows the plot of $(2{\cdot}303 \Sigma V \Delta \log_{10} c)/A$ against $t$ for one run with each type of centre stud. The origin for one run is displaced to distinguish the experimental points.

TABLE 1.

| | $k_T$ (obs.) (cm./min.) |
|---|---|
| Perspex stud ..... | 0·161, 0·159, 0·157, 0·156, 0·153, 0·158, 0·157, 0·160, 0·155; mean, 0·157 |
| Zinc stud ..... | 0·152, 0·157, 0·157, 0·155, 0·157, 0·157, 0·160, 0·164; mean, 0·157 |

*Rate of Stirring.*—The effect of varying the rate of stirring was studied at 25° over the range 73—292 r.p.m., Perspex centre studs being used. In each case, the rate of stirring was maintained constant by means of the stroboscope and manual control described previously.[14] The observed values of $k_T$ are recorded in Table 2.

*Temperature Coefficient and Kinematic Viscosity.*—The rate of reaction was studied at six temperatures over the range 20—45°, Perspex centre studs and stirring at 146 r.p.m. being used.

The kinematic viscosity of the solution was measured at each temperature by means of an Ostwald viscometer. The appropriate kinetic energy correction was applied by means of Barr's method.[16] The results are shown in Table 3.

TABLE 2.

| Rate of stirring (r.p.m.) | $k_T$ (obs.) (cm./min.) | Mean $k_T$ (cm./min.) |
|---|---|---|
| 73 | 0·116, 0·118 | 0·117 |
| 109 | 0·142, 0·141, 0·141, 0·136 | 0·140 |
| 146 | (See Table 1) | 0·157 |
| 219 | 0·193, 0·192 | 0·193 |
| 292 | 0·220, 0·224 | 0·222 |

TABLE 3.

| Temp. | $k_T$ (obs.) (cm./min.) | Mean $k_T$ (cm./min.) | $10^5\nu$ (cm.$^2$/sec.) |
|---|---|---|---|
| 20·0° | 0·146, 0·142, 0·142, 0·143, 0·144 | 0·143 | 9·95 |
| 25·0 | — | 0·157 | 8·72 |
| 30·0 | 0·173, 0·169, 0·175, 0·173, 0·173 | 0·173 | 7·98 |
| 34·9 | 0·193, 0·195, 0·191, 0·189 | 0·192 | 7·15 |
| 39·9 | 0·209, 0·209, 0·204, 0·207 | 0·207 | 6·52 |
| 44·9 | 0·225, 0·224, 0·220, 0·220, 0·220 | 0·222 | 5·97 |

*Coefficient of Diffusion.*—Diffusion coefficients were determined by using Stokes's modification of the sintered-pad technique,[17] the only important difference being that cells with ground-glass joints were used since the rubber bungs used by Stokes would absorb iodine. The ground joints were lightly greased with a heavy lithium stearate wax, which proved quite satisfactory and did not penetrate into the pad. A solution of iodine dissolved in 0·08N-potassium iodide was placed in the lower compartment, and allowed to diffuse into potassium iodide of the same concentration. Duplicate determinations generally agreed to within 1%, and thus were sufficiently accurate for the purpose of this investigation. Within the limits of experimental error, no significant change in $D$ was observed on varying the initial concentration of iodine over the range 0·01—0·07N. The observed values of $D$ for solutions initially *ca.* 0·05N in iodine are recorded in Table 4.

TABLE 4.

| Temp. | $10^5D$ (obs.) (cm.$^2$/sec.) | $10^5D$ (mean) (cm.$^2$/sec.) | Temp. | $10^5D$ (obs.) (cm.$^2$/sec.) | $10^5D$ (mean) (cm.$^2$/sec.) |
|---|---|---|---|---|---|
| 25·0° | 1·14, 1·15 | 1·15 | 40·0° | 1·62, 1·63 | 1·63 |
| 30·0 | 1·31, 1·32 | 1·32 | 45·0 | 1·80, 1·78 | 1·79 |
| 35·0 | 1·47, 1·47 | 1·47 | | | |

## DISCUSSION

The apparent area of the working surface, $A$, must be known before values of the unit rate constant, $k_T$, can be calculated from the experimental data. For the present system, the usual method of mounting the discs on the stirring shaft gave an inert patch of Perspex at the centre of the working surface. The exposed area of the centre stud was *ca.* 4% of the total area, whilst the experimental method is sensitive to changes in $k_T$ of the order of 2%, so that it might at first sight appear necessary to subtract the area of the Perspex from the total apparent area of the surface. However, as shown by the results reported in Table 1, and by the two experimental plots shown in Fig. 2, there is no difference to be discerned in the observed rate when the Perspex centre stud is replaced by one of zinc. There can be little doubt that it is the total apparent area of the underside of the disc which must be used. All the reported values of $k_T$, including those in Table 1, have been computed on this basis.

There is an interesting explanation of this effect. Since the rate of reaction is solely determined by the rate at which iodine can be transported to the working surface, the zinc surface is capable of reducing iodine at a faster rate than that at which it is supplied. Iodine reaching the inert Perspex stud is thrown outwards along the surface of the disc,*

* See ref. 1, Fig. 3.

[15] Bradley, *Trans. Faraday Soc.*, 1938, **34**, 278.
[16] Barr, "A Monograph of Viscometry," Clarendon Press, 1931.
[17] Stokes, *J. Amer. Chem. Soc.*, 1950, **72**, 763, 2243; 1951, **73**, 3527.

and is consumed in the surface reaction before reaching the outer edge of the disc. For a given solution, temperature, and rate of stirring, the maximum rate at which iodine can be transported to the disc is determined solely by the overall area of the disc, so that, provided the inert centre stud is relatively small, the rate of the surface reaction will nowhere reach the saturation value. As it would clearly be of interest to investigate the effect of progressively enlarging the inert centre patch, a study has been made for the reaction between copper and acidified dichromate solutions.[18]

The opposite effect was observed when a small pin-hole appeared in the lacquer protecting the upper surface of the disc. Although the increase in the exposed area was quite negligible, an appreciable increase in rate was observed. In normal circumstances, there is no concentration gradient set up at the upper, protected surface. Once a pin-hole appears in the lacquer, the exposed area of zinc is supplied with iodine at a very fast rate, and reaction becomes rapid. This argument is borne out in practice by the observation that a very deep pit is etched under such flaws in the lacquer, and it emphasises the need for extreme care when blocking off non-working areas.

FIG. 3.

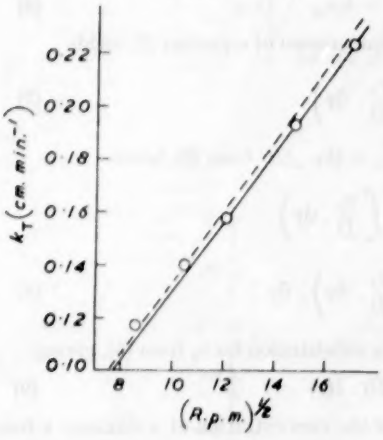
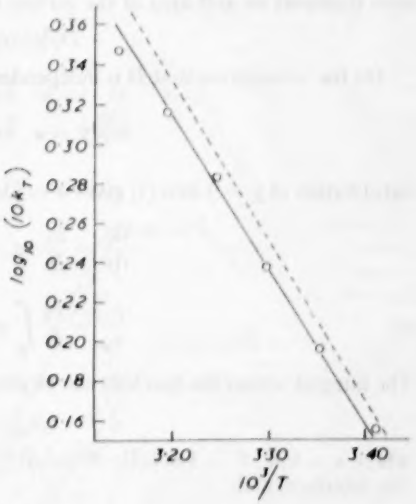



FIG. 4.




We turn now to the effect of varying the rate of stirring. Fig. 3 shows the mean value of $k_T$ at each speed plotted against the square root of the rate of stirring. The three points corresponding to 146, 219, and 292 r.p.m. fall accurately on a straight line passing through the origin; the points for 73 and 109 r.p.m. are slightly higher. A possible explanation is that natural convection is making an appreciable contribution to the transport process under these conditions for, in practice, the limiting value of $k_T$ as $\omega$ approaches zero is finite, not zero. The correct explanation, however, is thought to be the onset of an edge effect at low speeds due to the rather thick foils used in preparing the discs. In a similar study of the rate of transport of dichromate ion to copper discs only *ca.* 0·15 mm. thick, the experimental points all fall accurately on a straight line passing through the origin.[18]

Of more interest is the fact that the best straight line through the points is significantly lower than the broken line, which was computed from equation (2) by using the values for $D$ and $\nu$ given in Tables 3 and 4. That Levich's theory predicts values which are too high is shown more clearly by Fig. 4, in which the logarithm of the mean value of $k_T$ at each temperature is plotted against the reciprocal of the absolute temperature; again, the broken line was computed from equation (2) by using the data given in Tables 3 and 4.

Since the data reported in Tables 2—4 are accurately represented by the relation

[18] Gregory and Riddiford, to be published.

$k_T \propto D^{2/3}\nu^{-1/6}\omega^{1/2}$ within the limits of experimental error,[19] the discrepancy lies in the number 0·620, and has been traced to an approximation made by Levich.

For the steady-state transport of mass in the system

$$D(\mathrm{d}^2c/\mathrm{d}y^2) = v_y(\mathrm{d}c/\mathrm{d}y) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where $c$ is the concentration of iodine at a distance $y$, measured normal to the plane of the disc ($y = 0$), and $v_y$ is the normal component of the fluid velocity.[1] The boundary conditions are :

$$\left.\begin{array}{llll} y = 0, & c = 0, & v_y = 0 & \\ y = \infty, & c = c_\infty, & v_y = -0{\cdot}886(\nu\omega)^{1/2} & \end{array}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The conditions for $v_y$ are due to Cochran,[4] who has shown that for small values of $y$

$$v_y = (\nu\omega)^{1/2}[-0{\cdot}510(\omega/\nu)y^2 + 0{\cdot}333(\omega/\nu)^{3/2}y^3 - 0{\cdot}103(\omega/\nu)^2y^4 + 0{\cdot}0127(\omega/\nu)^{5/2}y^5 + 0{\cdot}00283(\omega/\nu)^3y^6 + \ldots] \quad . \quad . \quad (5)$$

From the boundary conditions (4), transport at $y = 0$ is purely diffusive, so that the rate of mass transport to unit area of the surface is given by

$$-D(\mathrm{d}c/\mathrm{d}y)_{y=0} = -k_Tc_\infty \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

On the assumption that $D$ is independent of $c$, integration of equation (3) yields

$$\mathrm{d}c/\mathrm{d}y = a \,.\, \exp\left(\int_0^y \frac{v_y}{D} \,.\, \mathrm{d}y\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Substitution of $y = 0$ into (7) gives $a = (\mathrm{d}c/\mathrm{d}y)_{y=0} = (k_Tc_\infty)/D$ from (6), hence

$$\frac{\mathrm{d}c}{\mathrm{d}y} = \frac{k_T}{D} \,.\, c_\infty \,.\, \exp\left(\int_0^y \frac{v_y}{D} \,.\, \mathrm{d}y\right)$$

or

$$\frac{c}{c_\infty} = \frac{k_T}{D}\int_0^y \exp\left(\int_0^y \frac{v_y}{D} \,.\, \mathrm{d}y\right) \,.\, \mathrm{d}y \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

The integral within the brackets can be obtained by substitution for $v_y$ from (5), giving

$$c/c_\infty = (k_T\delta'/D) \,.\, \mathrm{I}(x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where $x = y/\delta'$, $\delta' = 1{\cdot}805(D/\nu)^{1/3}(\nu/\omega)^{1/2}$, $c$ is now the concentration at a distance $x$ from the interface, and

$$\mathrm{I}(x) = \int_0^x \exp\left[-x^3 + 0{\cdot}885(D/\nu)^{1/3}x^4 - 0{\cdot}394(D/\nu)^{2/3}x^5 + 0{\cdot}729(D/\nu)x^6 + \ldots\right]\mathrm{d}x$$

Then

$$k_T = D/[\delta' \,.\, \mathrm{I}(\infty)] = (0{\cdot}554D^{2/3}\nu^{-1/6}\omega^{1/2})\mathrm{I}(\infty) \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The problem therefore reduces to the evaluation of the integral $\mathrm{I}(\infty)$. Also, from equations (9) and (10),

$$c/c_\infty = \mathrm{I}(x)/\mathrm{I}(\infty) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

from which the distribution of concentration can be determined.

Levich pointed out that when $y \gg \delta'$, $x \gg 1$, so that, since $(D/\nu) \sim 10^{-3}$ for solutions at room temperature, the integral converges rapidly. He regards $\delta'$ as the thickness of the boundary layer over which a concentration gradient exists. He assumed that the convergence is so rapid that terms in $x^4$ and above may be neglected, *i.e.*, that

$$\mathrm{I}(\infty) = \int_0^\infty \exp(-x^3) \,.\, \mathrm{d}x = \Gamma(4/3) = 0{\cdot}8934$$

which, with equation (10), gives equation (2).

[19] Gregory, Ph.D. Thesis, Southampton, 1955.

FIG. 5.

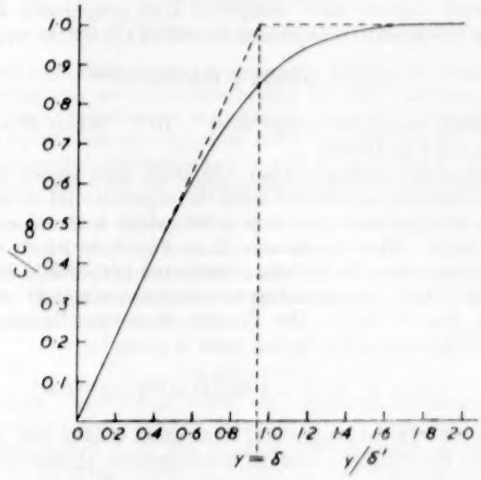
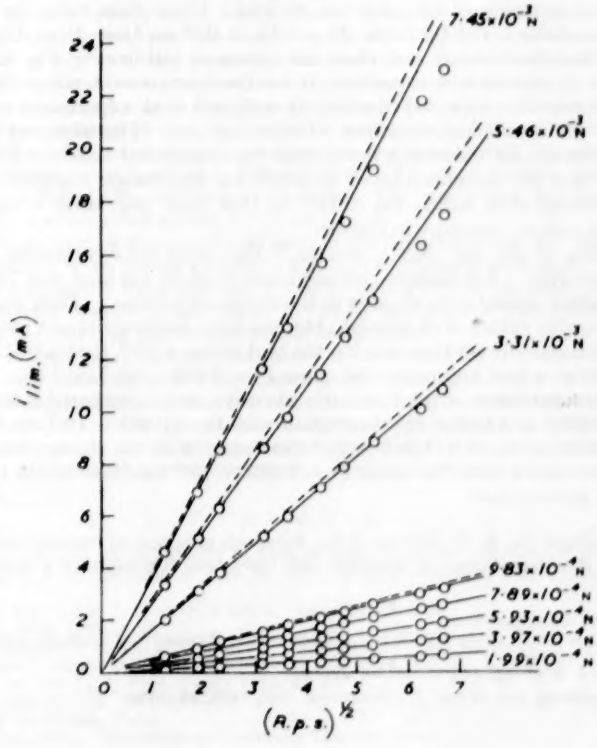

1·0
0·9
0·8
0·7
0·6
0·5
0·4
0·3
0·2
0·1
C/C₀
0 0·2 0·4 0·6 0·8 1·0 1·2 1·4 1·6 1·8 2·0
y = δ
y/δ'

FIG. 6.


7·45×10⁻³N
5·46×10⁻³N
3·31×10⁻³N
9·83×10⁻⁴N
7·89×10⁻⁴N
5·93×10⁻⁴N
3·97×10⁻⁴N
1·99×10⁻⁴N
i/10 (mA)
0 1 2 3 4 5 6 7
(R.p.s.)½

A closer examination shows, however, that the term in $x^4$ makes a significant contribution to the integral. The term in $x^5$ is very small, and the higher terms can be neglected. The present authors have computed $I(\infty)$ graphically for several values of $D/\nu$, and find that the results can be expressed to within 1% by the equation

$$I(\infty) = 0{\cdot}8934 + 0{\cdot}316(D/\nu)^{0{\cdot}36} \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

for values of $D/\nu$ falling within the range 0—$4 \times 10^{-3}$. When $D/\nu = 10^{-3}$, $I(\infty)$ is 3% higher than the value used by Levich.

By using the appropriate values of $I(\infty)$, the solid lines shown in Figs. 3 and 4 were obtained, showing satisfactory agreement with the experimental data. For the values of $D/\nu$ investigated, the integral converges at $y = 2\delta'$, which is therefore the thickness of the transport boundary layer. This can be seen from Fig. 5, in which the variation of concentration with distance normal to the disc, computed graphically from equation (11), is shown for $D/\nu = 3{\cdot}08 \times 10^{-3}$, corresponding to a temperature of 45° in the present system. The broken line in Fig. 5 shows the Nernst slope (or "equivalent concentration profile"[20]); * $\delta$, the thickness of the Nernst layer is given by

$$\delta = \delta' \, . \, I(\infty) = 1{\cdot}805(D/\nu)^{1/3}(\nu/\omega)^{1/2}I(\infty)$$

It is of interest to see how far Hogge and Kraichman's data can be correlated by the extended theory, since their electrochemical investigations should be of greater precision than the corrosive study reported in the present paper. Their observed limiting currents for the reduction of tri-iodide ion at a rotating platinum disc cathode [8] are shown plotted against the square root of the speed of rotation in Fig. 6. The numbers shown on the plot refer to the concentrations of tri-iodide ion studied. Using their value for the kinematic viscosity of the solution, and the value $D = 1{\cdot}15 \times 10^{-5}$ cm.$^2$/sec. from Table 4, we have computed the theoretical slopes and these are shown as full lines in Fig. 6. The broken lines have been computed from equation (1) for the four concentrations indicated. The agreement between the extended theoretical equation and experiment is satisfactory, particularly at the lower concentrations of tri-iodide ion. The observed results at the higher concentrations are somewhat lower than the theoretical values. This is probably due to the fact that the concentration of tri-iodide ion is no longer negligible in comparison with the concentration of iodide ion (0·1N), so that ionic migration is causing a slight reduction in the rate of transport to the disc.

In their study of the $Ag^+$–$KNO_3$ system,[19] they used 0·2N-potassium nitrate as the supporting electrolyte. The highest concentration of silver ion used was $7{\cdot}47 \times 10^{-4}$N, so that ionic migration should play no part in the transport process. Their data can be used to check how rapidly values of $D$ may be obtained from limiting-current measurements by cyclic approximation. From their results, the best value of $D^{2/3}/I(\infty)$ is $6{\cdot}515 \times 10^{-4}$. Use of $I(\infty) = 0{\cdot}8934$ as a first approximation gives $D = 1{\cdot}405 \times 10^{-5}$ cm.$^2$/sec. This, coupled with their determined value of the kinematic viscosity, and substituted into equation (12), gives $I(\infty) = 0{\cdot}9255$ as a better approximation with $D = 1{\cdot}480 \times 10^{-5}$ cm.$^2$/sec. Repetition of the process gives $D = 1{\cdot}482 \times 10^{-5}$ cm.$^2$/sec., with no change thereafter. This value may be compared with the value $D = 1{\cdot}485 \times 10^{-5}$ cm.$^2$/sec. which they computed from Onsager's limiting law.

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* Ref. 1, Fig. 1, is wrong, and should be ignored.

[20] Tobias, Eisenberg, and Wilke, *J. Electrochem. Soc.*, 1952, **99**, 359c.

## 732. *The Viscosity and Intermolecular Potential of Silicon Tetrafluoride.*

By C. P. Ellis and C. J. G. Raw.

A modified form of transpiration apparatus, adapted for relative determinations involving only small volumes of gas, has been used to determine the viscosity of silicon tetrafluoride in the range 20—140°. The results are well represented by Sutherland's equation (with $C = 151°$ K), and the Lennard-Jones (12,6) potential parameters ($\varepsilon/k = 147°$ K; $\sigma = 5{\cdot}13$ Å) have been computed and compared with the values obtained from second virial coefficients.

The recent researches in these laboratories on the viscosity and intermolecular potential of boron trifluoride [1,2] led the authors to consider the gas silicon tetrafluoride whose properties are very similar. Although the second virial coefficient [3] has been determined and used to evaluate the intermolecular potential energy, the literature appears to lack data on the viscosity of silicon tetrafluoride.

### Experimental

*Preparation of Silicon Tetrafluoride.*—This was prepared by heating barium hexafluorosilicate to about 500° in an electric furnace (Bairar *et al.*[4]). Purification by vacuum-distillation of the gas after it had passed from the reaction tube through an ethanol–carbon dioxide trap, was effected in an all-glass apparatus similar to that described by Germann and Booth.[5]

*Viscometer.*—In principle the apparatus is similar to Schultze's transpiration apparatus,[6] but a number of simplifying modifications have been introduced.

With the exception of rubber pressure tubing between the mercury reservoirs and the gas containers, it is made wholly from Pyrex glass. After the gas had been introduced, the levels in the multiplying manometers were adjusted at an equal height above and below the original level, so as to give a fixed pressure difference across the capillary tube. The taps isolating the capillary tube from the manometers and mercury reservoirs on either side were opened, and the gas was allowed to flow through a thin-walled spiral preheater and the capillary tube (length 33 cm., radius 0·01 cm.), both of which were contained in an oil-thermostat (±0·2°). The levels of the liquid in the multiplying manometers, and consequently the pressure differences, were kept unaltered throughout each determination. This was possible owing to the slow passage of the gas through the narrow-bore capillary. The time of flow of a fixed volume of gas (approx. 34 c.c.) was measured correct to 0·2 sec.

The multiplying manometers employed were of the type described by Higgins.[7] They increase the sensitivity of an ordinary mercury manometer approximately eight times.

The mercury reservoirs were operated manually through reduction gears situated close together at bench level to allow of their being turned by the operator whilst observing the levels of the liquid in the centrally placed multiplying manometers.

The use of a fixed volume of gas eliminated the necessity for withdrawing and weighing mercury after each determination. The maintenance of the manometer levels at a constant difference for all experiments obviated any error due to changes of atmospheric pressure.

*Calculation of Results.*—The apparatus was calibrated with pure dry air in the range 20—150°. By using the observed time of flow measurements in conjunction with the published mean results [8] for the viscosity of air at the same temperatures, a constant for the apparatus was obtained from the formula :

$$k' = (\eta_1 - \eta_2)/(t - t_2) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $k'$ is the constant for *differences* in temperature, $\eta_2$ is the viscosity of air at a standard temperature (23°), $t_2$ is the time of flow in seconds at a standard temperature, and $\eta_1$ and $t$

[1] Cooke and Mackenzie, *J. S. African Chem. Inst.*, 1951, **4**, 123.
[2] Raw, *ibid.*, 1954, **7**, 20.
[3] Hamann, McManamey, and Pearse, *Trans. Faraday Soc.*, 1953, **49**, 351.
[4] Bairar *et al.*, "Inorganic Syntheses," McGraw Hill, 1953, Vol. IV, p. 145.
[5] Germann and Booth, *J. Phys. Chem.*, 1917, **21**, 81.
[6] Schultze, *Ann. Physik*, 1901, **5**, 140.
[7] Higgins, M.Sc. Thesis, Natal.
[8] Landolt-Börnstein, "Physikalisch Chemische Tabellen."

represent the viscosity and time of flow at other temperatures. The value of $k'$ was found experimentally to be 0·947 for this viscometer.

The viscosity of air at 23° has been determined with particular accuracy, and a weighted mean viscosity of $1830 \times 10^{-7}$ g. cm.$^{-1}$ sec.$^{-1}$ assigned to it.[9] This was consequently selected as the standard.

In these experiments the pressure difference was held constant for all readings, the same volume of gas was used throughout, the radius and length of the capillary also remained constant, hence Poiseuille's formula [10] reduces to

$$\eta_a = kt_a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $k$ is the apparatus constant for a particular temperature—in this case 23°. At 23° the average rate of flow for dry air was found to be 678·0 sec., whence $k = 2{\cdot}700 \times 10^{-7}$.

For the range of temperatures employed, the slip effect is less than the experimental accuracy of about 0·5% and it has been neglected in these experiments.

## Results and Discussion

From results obtained in the case of silicon tetrafluoride the rate of flow at 23° was found to be 563·0 sec. Whence, by use of eqn. (2), $\eta_a = 1520 \times 10^{-7}$ g. cm.$^{-1}$ sec.$^{-1}$. The experimental results obtained are recorded in the Table, where $\eta$ is calculated at the higher temperatures by using equation (1).

*Variation of viscosity of silicon tetrafluoride with temperature.*

| Temp., $T$ (°K) | $t - t_a$ | $\eta - \eta_a$ | $\eta \times 10^7$ (g. cm.$^{-1}$ sec.$^{-1}$) | $T^{3/2}/\eta$ | Temp., $T$ (°K) | $t - t_a$ | $\eta - \eta_a$ | $\eta \times 10^7$ (g. cm.$^{-1}$ sec.$^{-1}$) | $T^{3/2}/\eta$ |
|---|---|---|---|---|---|---|---|---|---|
| 296·0° | ($t_a$ = 563) | — | 1520 | 3·351 | 352·5° | 239·6 | 226·9 | 1747 | 3·787 |
| 304·3 | 35·6 | 33·70 | 1554 | 3·416 | 362·8 | 285·6 | 270·4 | 1790 | 3·860 |
| 313·1 | 77·4 | 73·28 | 1593 | 3·477 | 373·1 | 327·5 | 310·1 | 1830 | 3·938 |
| 321·8 | 105·2 | 99·61 | 1620 | 3·563 | 383·5 | 371·8 | 352·1 | 1872 | 4·013 |
| 332·1 | 147·0 | 139·2 | 1695 | 3·647 | 394·1 | 417·5 | 395·3 | 1915 | 4·091 |
| 342·4 | 194·4 | 184·1 | 1704 | 3·718 | 406·8 | 477·0 | 451·6 | 1972 | 4·161 |

Sutherland's equation for the variation of the viscosity of a gas with temperature can be written [10] in the form, $T = (AT^{3/2}/\eta) - C$, where $A$ and $C$ are constants; $C$ can be obtained as the negative intercept on the $T$-axis if $T$ is plotted against $T^{3/2}/\eta$.

From a plot of the values given in the Table, $C$ for silicon tetrafluoride is found to be 151° K.

The viscosity can be used, following Hirschfelder *et al.*,[11] to obtain the parameters in the empirical Lennard-Jones (12,6) form of the intermolecular potential energy. By trial-and-error values of these, potential parameters are chosen which on substitution in the theoretical equation for the viscosity give values in agreement with the experimental results. The potential parameters determined in this way have values $\varepsilon/k = 147°$ K and $\sigma = 5{\cdot}13$ Å, where $\varepsilon$ is the depth of the potential well, $\sigma$ is the collision diameter (the separation for which the potential energy is zero), and $k$ is Boltzmann's constant.

The results obtained by Hamann *et al.*[3] from second virial coefficients are $\varepsilon/k = 147{\cdot}8°$ K and $\sigma = 5{\cdot}95$ Å. The discrepancy in the case of the collision diameter is no doubt due to the inadequacy of the Lennard-Jones model in describing different properties by using the same potential parameters.

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University of Natal, Pietermaritzburg, South Africa. [*Received, May 14th*, 1956.]

[9] Kaye and Laby, "Physical and Chemical Constants," Longmans Green and Co., London, 10th edn., 1948.
[10] Partington, "Advanced Treatise on Physical Chemistry," Longmans Green and Co., Vol. I, 1949.
[11] Hirschfelder, Curtiss, and Bird, "Molecular Theory of Gases and Liquids," Wiley, New York, 1954.

## 733. *Chemistry of the Higher Fungi. Part VI.* Isomerisation Reactions of Naturally Occurring Allenes.*

By J. D. Bu'Lock, E. R. H. Jones, P. R. Leeming, and J. M. Thompson.

When treated with alkali, nemotinic acid and nemotin both undergo prototropic rearrangements resulting in the disappearance of the allene groups. Nemotinic acid gives (−)-4-hydroxyundeca-6 : 8 : 10-triynoic (*iso*-nemotinic) acid, but with nemotin the isomerisation involves opening of the lactone ring and gives undec-4-ene-6 : 8 : 10-triynoic acid (nemotin A). The latter is also obtainable by treatment of the lactone of *iso*nemotinic acid with alkali. Reasons for the different behaviour in alkali of the known naturally occurring allenes are considered.

One of the most striking properties of the antibiotics nemotinic acid and nemotin described in the original papers [1] was their instability towards aqueous alkali. The neutral compound, nemotin, with the absorption spectrum of an enediyne, was rapidly converted at pH 10 into nemotin A, thought to be a neutral compound,[1] with the ultraviolet absorption spectrum of an enetriyne.[1a] The conjugated unsaturation of the molecule thus increased by two double-bond equivalents; the change in light absorption spectrum is most conspicuous (cf. Table 1) as new bands of high intensity appear. The behaviour in aqueous alkali of nemotinic acid (having the same chromophore as nemotin) was quite different; in a much slower reaction, the specific absorption of nemotinic acid gradually disappeared, without any new bands appearing in the spectrum. No reaction product was isolated.

Table 1. *Ultraviolet absorption spectra.*

| Substance | Absorption max. (Å) and log ε (in parentheses) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Nemotin | — | — | 2085 (4·74) | — | 2365 (3·79) | 2490 (4·03) | 2625 (4·19) | 2780 (4·09) | — | — |
| Nemotin A | 2045 (4·41) | 2115 (4·37) | 2230 (infl.) (4·47) | 2300 (4·77) | 2410 (4·93) | 2580 (3·44) | 2720 (3·78) | 2885 (4·07) | 3070 (4·19) | 3280 (4·04) |
| Methyl nemotin A | 2045 | 2120 | 2230 (infl.) | 2300 | 2410 | 2570 | 2720 | 2880 | 3070 | 3280 |
| | — | — | — | — | — | — | — | — | — | — |
| *iso*Nemotinic acid | | | 2075 (5·05) | — | 2390 (2·34) | 2540 (2·45) | 2685 (2·56) | 2850 (2·56) | 3050—3080 (2·40) | — |
| *iso*Nemotinic lactone | — | — | 2060 (5·11) | — | 2400 (2·16) | 2530 (2·28) | 2680 (2·42) | 2850 (2·41) | 3040 (2·20) | — |

Publication [2] in 1952 of the work of Celmer and Solomons on mycomycin and its rearrangement in alkali to *iso*mycomycin provided support for the idea that nemotinic acid and nemotin might owe their high optical activity and alkali-instability to the presence of allene groups, a view which was confirmed when we showed these compounds to be (I) and (II) respectively.[3] However, detailed investigation of their isomerisations has revealed that these are not fully analogous to the rearrangement of mycomycin.

When nemotinic acid is treated with alkali (0·1N-sodium hydroxide) a product, *iso*-nemotinic acid, can be isolated from the neutralised solution by ether-extraction. After purification, this acid shows the absorption spectrum of a conjugated triyne (Table 1); the maxima are of such low intensity that they are easily masked and were consequently not observed by the earlier workers. The product forms colourless, highly photosensitive needles; it is optically active ($[\alpha]_D^{20}$ −3°) but its specific rotation is very much less than that of nemotinic acid ($[\alpha]_D^{20}$ +320°). Apart from the absence of the sharp allene peak at 1960 cm.$^{-1}$, it shows infrared absorption very similar to that of nemotinic acid. Bands

* Part V, Bu'Lock, Jones, and Leeming, *J.*, 1955, 4270.

[1] Anchel, Polatnick, and Kavanagh, *Arch. Biochem.*, 1950, **25**, 208; Kavanagh, Hervey, and Robbins, *Proc. Nat. Acad. Sci. U.S.A.*, 1950, **36**, 1.

[1a] Anchel, *J. Amer. Chem. Soc.*, 1952, **74**, 1588.

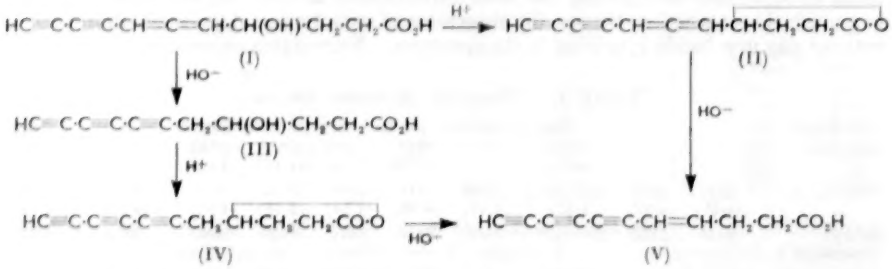
[2] Celmer and Solomons, *J. Amer. Chem. Soc.*, 1952, **74**, 1870, and later papers.

[3] Bu'Lock, Jones, and Leeming, *J.*, 1955, 4270.

ascribed to hydroxyl and acetylenic hydrogen in the case of nemotinic acid are also present in the infrared spectra of *iso*nemotinic acid and its methyl ester. Like nemotinic acid, *iso*nemotinic acid is readily lactonised; the crystalline, optically active lactone ($[\alpha]_D^{20}$ −3·5°) has in its infrared absorption spectrum a carbonyl band at 1795 cm.$^{-1}$, indicative of a saturated γ-lactone ring. Hydrogenation of *iso*nemotinic acid and distillation of the product gives (+)-γ-undecanolactone (identified as 4-oxoundecanamide).

*iso*Nemotinic acid is clearly (−)-4-hydroxyundeca-6 : 8 : 10-triynoic acid (III) and its lactone is (IV).

The reported formation of a neutral enetriyne from nemotin [1] was difficult to reconcile with structure (II) for the latter; however, when the conversion of nemotin into nemotin A was repeated, it was found that the crystalline enetriyne (ultraviolet absorption spectrum, Table 1) was a carboxylic acid, with p$K_a$ 4·70 (*i.e.*, not αβ-unsaturated). Though nemotin A is quite photosensitive, it proved to be the most easily handled compound of this series and gave reasonably good analyses for $C_{11}H_8O_2$; this is important as it may be prepared indirectly from nemotinic acid as well as from nemotin and so characterises both compounds. The infrared spectra of nemotin A and its methyl ester show the acetylenic hydrogen band at 3280 cm.$^{-1}$ and carbonyl bands at 1708 and 1742 cm.$^{-1}$ respectively, but no allene or hydroxyl band is present; nemotin A has no measurable optical activity. Hydrogenation converts nemotin A into undecanoic acid directly, so that nemotin A must be undec-4-en-6 : 8 : 10-triynoic acid (V).




Just as the conversion of nemotinic acid into its lactone, nemotin, helped in establishing the structures (I) and (II) for these compounds, so it seemed desirable to correlate their isomerisation products in some way. *iso*Nemotinic acid is apparently stable in aqueous 0·1N-alkali, but it has been found that the derived lactone (IV) gives nemotin A in up to 40% yield under alkaline conditions. The remainder of the lactone is apparently hydrolysed back to *iso*nemotinic acid; nemotin A was isolated from the reaction mixture by countercurrent distribution and characterised spectroscopically as the methyl ester.

The alkali-catalysed isomerisation reactions of mycomycin, nemotinic acid, and nemotin are three variants of the simple allene-acetylene rearrangement, $-CH{=}C{=}CH- \rightleftharpoons -CH_2{\cdot}C{\equiv}C-$, which has been extensively studied by various workers.[4] The mycomycin ⟶ *iso*mycomycin change involves the migration of two protons, the isomerisation of nemotinic acid is a simple prototropic change, and the conversion of nemotin into nemotin A combines the rearrangement with an elimination. These diverse reactions can be reconciled by consideration of the initial step, which in every case is presumably the removal of a proton from the allene group. Of the two allenic hydrogen atoms, that which is the more acidic will be removed preferentially. Thus in the isomerisation of nemotinic acid (Fig. 1), the hydrogen atom *b* is allylic only to an enediyne system, whereas the other (*a*) is allylic both to the diyne group and to a double bond. Consequently the latter is removed and rearrangement proceeds as shown. In the rearrangement of mycomycin (Fig. 2) hydrogen atom *a* is allylic to diyne and triene groups, and hydrogen atom *b* is allylic to enediyne and diene groups; removal of the latter gives the more highly conjugated anion (the diyne

[4] Jacobs, Akawie, and Cooper, *J. Amer. Chem. Soc.*, 1951, **73**, 1273; Eglinton, Jones, Mansfield, and Whiting, *J.*, 1954, 3197 *et seq.*

system being considerably less polarisable than the enediyne system) and so in mycomycin this is the initial point of attack, the rearrangement of the cumulene intermediate probably proceeding as shown. In the isomerisation of nemotin the first step involves the same hydrogen atom as in nemotinic acid (Fig. 3), but the subsequent course of the reaction is determined by the elimination of the neighbouring oxycarbonyl group, so that nemotin A is formed as shown. Such an effect would be much less likely in the case of nemotinic acid

FIG. 1.

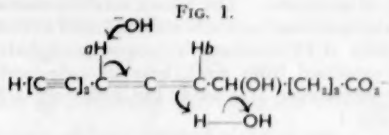


FIG. 2.

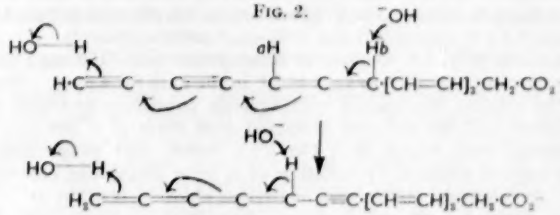
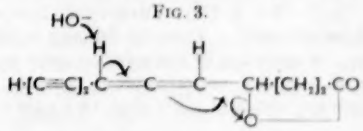


FIG. 3.



because of the lower electronegativity of the hydroxyl compared with the oxycarbonyl group; in fact only a minute amount (<1%) of nemotin A could be detected in the isomerised nemotinic acid, and this may well have been formed from traces of nemotin present in the starting material. The absence of this effect in the isomerisation of nemotinic acid may partly explain its greater stability to alkali; another factor tending to slow down the isomerisation is that it requires the approach of two anions, whereas in the isomerisation of nemotin only one of the reacting entities is charged. (The relative alkali-stabilities of nemotinic acid and nemotin may be assessed from the data in Table 2.) The isomeris-

TABLE 2. *Effect of* pH *on allene isomerisation rates.*

| Reaction medium | | Buffer, pH 8·4 | Buffer, pH 10 | M/20-NaOH |
|---|---|---|---|---|
| Approx. time (min.) for 50% isomerisation | Nemotin ..... | 23 | 3 | <0·1 |
| | Nemotinic acid | — | — | 7 |

ation of *iso*nemotinic lactone to nemotin A can be formulated as a simple elimination following removal of the propargylic hydrogen atom. From the infrared spectra of the products, it appears that both reactions leading to nemotin A give mainly the *trans*-isomer; this accords with the reaction schemes outlined above. The reactions leading to nemotin A are to some extent analogous to those in which certain lactones [5] and β-acyloxy-esters [6] afford *trans*-αβ-unsaturated acids on treatment with alkali; in such reactions protons are removed from positions activated by alkoxycarbonyl groups. In the reactions at present under consideration the removable protons are in allylic (or propargylic) positions; the reactions proceed under far milder conditions.

In conclusion we would like to add that the statement, attributed to us in a recent review,[7] that nemotinic acid gives nemotin A on treatment with alkali, is of course incorrect.

[5] Pavly and Will, *Annalen*, 1918, **416**, 1.
[6] Linstead, Owen, and Webb, *J.*, 1953, 1211.
[7] Bohlmann, *Angew. Chem.*, 1955, **67**, 389.

## Experimental

For details of general experimental methods, see Part V.[3]

*Isomerisation of Nemotinic Acid.*—A solution of the acid (560 mg.) in ether was shaken with 0·1N-sodium hydroxide (500 + 250 c.c.), and the combined aqueous layers were kept for 2 hr. at 20°. The ultraviolet absorption of the solution then showed no further change and indicated the presence of about 1% of enetriyne. The brown solution was acidified and extracted with ether (3 × 250 c.c.), and the combined extracts were reduced in bulk and subjected to counter-current distribution between M/15-disodium hydrogen phosphate and ether. The purified *iso*nemotinic acid (III) crystallised from methylene chloride–pentane at −80° as colourless needles, rapidly becoming purple even at −40° in the dark, $[\alpha]_D^{20}$ −3° (*c* 1), p$K_a$ (in water) 4·75; ultra-violet absorption, Table 1.

*Methyl* iso*Nemotinate.*—*iso*Nemotinic acid (20 mg.) in ether was treated with a slight excess of distilled diazomethane in ether. The product was an oil, showing infrared absorption peaks at 3625 and 3470 cm.$^{-1}$ (O–H stretching) and 1737 cm.$^{-1}$ (ester-carbonyl).

iso*Nemotinic Lactone* (IV).—A solution of *iso*nemotinic acid (150 mg.) and sulphuric acid (3 c.c.) in pure dry dioxan (100 c.c.) was kept at 20° in the dark for 4 days. Water (100 c.c.) was then added and the solution neutralised with aqueous potassium hydrogen carbonate; more water (2 l.) was added and the solution extracted with ether (3 × 250 c.c.). The combined extracts were washed with water (2 × 150 c.c.), dried, and evaporated to small bulk, the product being kept in solution by addition of a little methylene chloride. iso*Nemotinic lactone* crystallised as colourless plates from methylene chloride–pentane at −70°; the crystals became pink in the dark at −40° and decomposed at 50° (Found: C, 75·6; H, 4·5. $C_{11}H_8O_2$ requires C, 76·7; H, 4·7%); $[\alpha]_D^{20}$ −3·5° (*c* 1·2); ultraviolet absorption, Table 1.

*Hydrogenations.*—(a) iso*Nemotinic acid.* The acid (50 mg.) in ethanol (20 c.c.) over platinum took up 5·6 mol. of hydrogen; evaporation of the solution gave an oil (47 mg.) with the odour of γ-undecanolactone. The oil, distilled under reduced pressure, had $n_D^{20}$ 1·4516, $[\alpha]_D^{20}$ +31° (*c* 1·1), and an infrared spectrum identical with that of (+)-γ-undecanolactone {$n_D^{20}$ 1·4540, $[\alpha]_D^{17}$ +29° (*c* 1·7)}.

(b) iso*Nemotinic lactone.* The lactone (65 mg.) in ethanol (25 c.c.) over platinum took up 5·7 mol. of hydrogen; the crude product showed $[\alpha]_D^{20}$ +24° (*c* 1·0) and after distillation showed bands at 1780 (strong) and 1710 cm.$^{-1}$ (weak). Ammonolysis of this mixture of (+)-γ-undecanolactone and undecanoic acid and oxidation of the product [3] yielded 4-oxoundecanamide (20 mg.), m. p. and mixed m. p. 130—131°.

*Isomerisation of Nemotin.*—A solution of nemotin (150 mg.) in ether was added to M/15-aqueous disodium hydrogen phosphate (400 c.c.), and the ether evaporated. After 16 hr. at 20°, when the ultraviolet absorption spectrum showed no further change, the solution was acidified and extracted with ether. The dried ether extracts were evaporated to dryness and the residue dissolved in ether–pentane; from this the *nemotin A* (V) crystallised at −70° as colourless photosensitive needles, decomp. 50—60° (Found: C, 76·7; H, 5·3. $C_{11}H_8O_2$ requires C, 76·7; H, 4·7%), p$K_a$ (in 20% aqueous ethanol), 4·70; ultraviolet absorption, Table 1; the compound was optically inactive.

*Hydrogenation of Nemotin A.*—The acid (48 mg.) in ethanol (25 c.c.) over platinum took up 6·6 mol. of hydrogen; evaporation of the solution yielded undecanoic acid (43 mg.), identified as the *p*-toluidide, m. p. and mixed m. p. 78°.

*Esterification of Nemotin A.*—The acid (10 mg.) and sulphuric acid (0·3 c.c.) in methanol (10 c.c.) was kept at 20° in the dark for 4 days. The mixture was poured into water and extracted with ether; the extract was washed with sodium hydrogen carbonate solution and water, then dried. The methyl ester (ultraviolet absorption, Table 1) showed infrared absorption at 1742 (ester-CO) and 3280 cm.$^{-1}$ (≡C–H) and no bands attributable to a hydroxyl group.

*Isomerisation of* iso*Nemotinic Lactone* (IV).—The lactone (30 mg.) in dioxan (60 c.c.) was added to 1% aqueous potassium carbonate (60 c.c.). After 90 min. at 20°, when the ultraviolet absorption of the solution showed no further change, the mixture was acidified, poured into water (2 l.) and extracted with ether (400 c.c.). The ether extract was washed with water (2 × 100 c.c.), and its ultraviolet absorption spectrum showed peaks ascribable to a mixture of an enetriyne and a triyne. The mixture was resolved by counter-current distribution in 4 tubes between ether and M/15-aqueous disodium hydrogen phosphate. When all the enetriyne had been eluted in the ether fractions these were combined and the product was esterified (as above)

with methanol–sulphuric acid. The ester showed ultraviolet and infrared absorption spectra identical with those of the methyl ester of nemotin A.

The authors are indebted to the Rockefeller Foundation for financial assistance, and to Glaxo Laboratories Ltd. for a maintenance grant (to P. R. L.). They are also grateful to Mr. E. M. Morton for microanalyses, to Miss W. Peadon and Mrs. J. Hopkins for spectroscopic measurements, and to Miss E. F. Leadbeater for all the mycological work.

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## 734. *Chemical Action of Ionising Radiations in Solutions. Part XVI.* Formation of Labile Phosphate Esters from Purine and Pyrimidine Ribonucleotides by Irradiation with X-Rays in Aqueous Solution.*

By M. DANIELS, G. SCHOLES, and J. WEISS.

Irradiation of purine and pyrimidine ribonucleotides in aqueous solution with *X*-rays (200 kv) results in the formation of intermediate labile phosphate esters which lead to a post-irradiation release of inorganic phosphate. This release of phosphate, which occurs after irradiation in the presence or absence of oxygen, follows a first-order rate law and is strongly base-catalysed. It is suggested that the radiation-induced lability of the nucleotides is due to the formation of activating carbonyl groups in the sugar components.

PREVIOUS studies [1] of the action of *X*-rays (200 kv) on purine and pyrimidine ribonucleotides in aqueous solutions have shown that a number of chemical reactions take place. Both the base and the pentose constituents are attacked, ammonia and inorganic phosphate being formed. Some free base is also liberated but no nucleoside or free pentose is produced. Such chemical changes induced by ionising radiations in dilute aqueous systems are due, in the first instance, to the production of free radicals from the water according to the net process : [2]

$$H_2O \longrightarrow H + OH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The radicals thus formed may then react with the solute. Because of the possible rôle of labile phosphate esters in the radiation-induced degradation of nucleic acids in aqueous systems,[3] we have studied the effects of *X*-rays on a number of phosphate esters. The ribonucleotides are of obvious interest from this point of view and in the following we report our observations with adenylic and cytidylic acid, which are typical of purine and pyrimidine ribonucleotides respectively.

### RESULTS

Irradiations were carried out on 0·1% (w/v) nucleotide solutions (~0·003M) adjusted to pH 6·6—7·0. In all cases, in addition to the formation of inorganic phosphate during irradiation, there was a post-irradiation release of inorganic phosphate, which at 25° and pH ~7 continued for about 30 hours. Hydrolysis of the labile ester was markedly base-catalysed, treatment with N-sodium hydroxide for 20—30 min. at room temperature being sufficient to liberate the phosphate completely; this alkali-lability provided a quick and convenient method for the estimation of this compound.

Figs. 1—3 show yield–dose plots for the production of inorganic phosphate and of the labile phosphate from aqueous solutions of the (commercial) nucleotides irradiated both in the presence and in the absence of oxygen. The labile material is a primary product of irradiation, as shown by the fact that the yield is initially proportional to the dose; the yields ($G$ = molecules/100 ev) are summarised in Table 1. For the purine-3′ and the pyrimidine-3′ nucleotide the yields of

* Part XV, *J.*, 1956, 832.

[1] Scholes and Weiss, *Exp. Cell. Res.*, 1952, *Suppl.* **2**, 219; *Biochem. J.*, 1953, **53**, 567.
[2] Weiss, *Nature*, 1944, **153**, 748; *Brit. J. Radiol.*, 1947, *Suppl.* **1**, 56.
[3] Scholes and Weiss, *Nature*, 1953, **171**, 920.

labile phosphate are decreased on removal of oxygen from the solution before irradiation; with adenosine-5′ phosphate about equal amounts are formed *in vacuo* and in the presence of oxygen. 3′- and 5′-Nucleotides differ in their dependence of yield of inorganic phosphate on radiation dose: with the (commercial) 3′-nucleotides there is an induction-like period, whereas the production of inorganic phosphate from the 5′-compound is initially a linear function of dose.

In solutions irradiated in the presence of oxygen, hydrogen peroxide could be readily

FIG. 1.

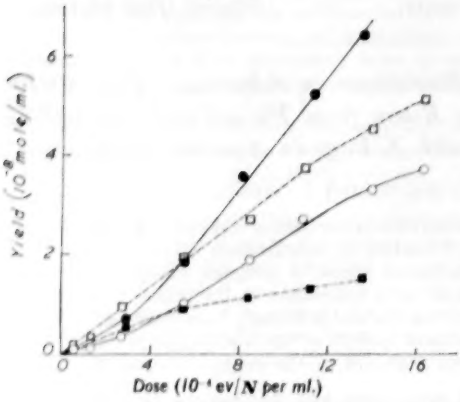



FIG. 2.

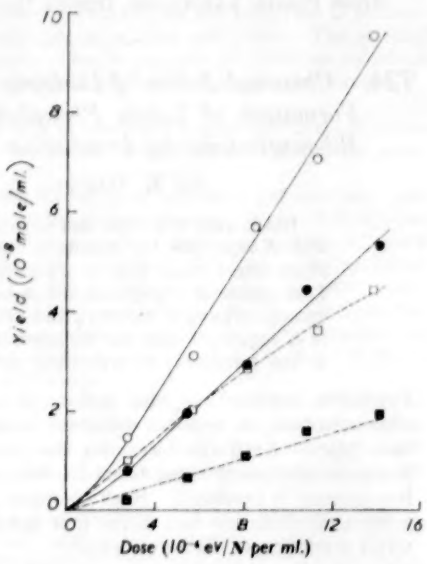
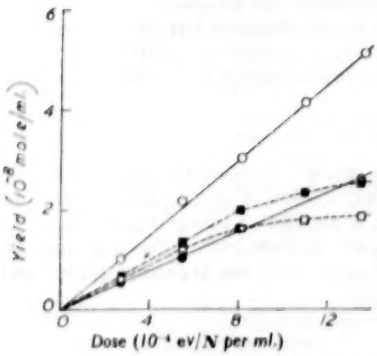



FIG. 3.




FIGS. 1—3. *Formation of inorganic phosphate and labile phosphate by X-irradiation (200 kv) of aqueous solutions (0·1% w/v) of (commercial) (Fig. 1) adenosine-3′ phosphate at pH 6·7, (Fig. 2) cytidine-3′ phosphate at pH 6·9, and (Fig. 3) adenosine-5′ phosphate at pH 6·6.*

*Inorganic phosphate* { ○ *in presence of oxygen (1 atm.).* ● in vacuo.

*Labile phosphate* ... { □ *in presence of oxygen (1 atm.).* ■ in vacuo.

detected: up to total doses of about $8 \times 10^{-6}$ ev/**N** per ml. there was a linear dependence and the initial yield $G(H_2O_2)$ was of the order of 1·5. *In vacuo*, on the other hand, much smaller quantities of peroxide were formed, in yields $[G(H_2O_2) \simeq 0{\cdot}5]$ comparable with the so-called "molecular yield."[4] Finally, the yields of hydrogen gas, in solutions irradiated *in vacuo*,

TABLE 1. *Initial yield of labile phosphate produced on irradiation of some ribonucleotides (commercial) in aqueous solution (0·1% w/v) with X-rays (200 kv) at pH = 6·6—7·0.*

| Nucleotide | Yield ($G$ = molecules/100 ev) In presence of $O_2$ (1 atm.) | *In vacuo* |
|---|---|---|
| Adenosine-3′ phosphate ..... | 0·34 | 0·18 |
| Cytidine-3′ phosphate ..... | 0·36 | 0·13 |
| Adenosine-5′ phosphate ..... | 0·23 | 0·25 |

were found to be initially linear with a smooth tail-off at higher doses; in all cases the initial yield $G(H_2)$ was $\simeq 1{\cdot}0$.

[4] Johnson and Allen, *J. Amer. Chem. Soc.*, 1952, **74**, 4147.

It has been found that the rate of post-irradiation release of inorganic phosphate follows a first-order law. Table 2 shows the values of the rate constants for this process at 25° and pH ~7; the rate is the same whether the solutions are irradiated in the presence of oxygen or *in vacuo*, indicating that the same labile product is produced under both conditions. One may conclude, on this evidence alone, that the production of an organic hydroperoxide ($RO_2H$) is not a necessary prerequisite for the formation of the labile material since, in general, hydroperoxides should only be formed if molecular oxygen is present during irradiation. It has been found, in the case of the purine nucleotides, that the same peroxide values are obtained by both the titanium and the iodide method of estimation. Since hydroperoxides, in general, can oxidise iodide but do not necessarily produce a colour with the titanium sulphate reagent, this suggests that no stable hydroperoxide is produced in these solutions. With cytidylic acid, on the other hand, irradiation in the presence of oxygen leads to the formation of a hydroperoxide ($G \simeq 0{\cdot}3$) which could be detected by this procedure; this indicates a specific effect due to the base and it is not unreasonable to suppose that the pyrimidine, but not the purine, can form a hydroperoxide.

None of these findings is compatible with the assumption that this post-irradiation release of phosphate is the result of a (slow) attack by the hydrogen peroxide in the solution on some relatively stable product of irradiation. If this was the case, phosphate liberation should take place according to second-order kinetics. The hydrogen peroxide does, in fact, disappear during the post-irradiation period but in accordance with a first-order law. In order to show conclusively that hydrogen peroxide is not responsible for the observed effect, experiments were carried out in which the hydrogen peroxide in the irradiated solution was removed by freeze-drying. Some typical results are recorded in Table 3. A single freeze-drying reduced

TABLE 2. *Rate constants (k) at 25° of post-irradiation release of inorganic phosphate from 0·1% (w/v) solutions of ribonucleotides (commercial) irradiated with X-rays (200 kv) at pH 6·8.*

| Nucleotide | $10^3k$ (min.$^{-1}$) | |
|---|---|---|
| | In presence of $O_2$ (1 atm.) | *In vacuo* |
| Adenosine-3′ phosphate ..... | 1·87 | 1·75 |
| Cytidine-3′ phosphate ..... | 2·05 | 2·06 |
| Adenosine-5′ phosphate ..... | 1·30 | 1·27 |

TABLE 3. *Freeze-drying experiments with solutions of adenosine-3′ phosphate (0·1% w/v) (commercial sample) irradiated with X-rays (200 kv) in the presence of oxygen (1 atm.). Total dose = $8{\cdot}4 \times 10^{-6}$ ev/N per ml. Hydrolyses carried out at pH 6·8 and 25°.*

| Irradiated solution | $H_2O_2$ ($10^{-6}$ mole per 100 ml.) | Inorganic phosphate before hydrolysis ($10^{-6}$ mole/100 ml.) | Inorganic phosphate after hydrolysis ($10^{-6}$ mole/100 ml.) | Rate of post-irradiation phosphate release ($10^3k$, min.$^{-1}$) |
|---|---|---|---|---|
| Untreated ..... | 12·5 | 1·9 | 4·1 | 1·87 |
| After 1st freeze-drying ..... | 2·0 | 2·0 | 4·15 | 1·80 |
| | 1·75 | 1·8 | 4·10 | — |
| After 2nd freeze-drying ... | 0·5 | 1·9 | 4·18 | 1·92 |

the hydrogen peroxide concentration to about one-sixth of its original value and a small quantity of " residual " peroxide remained after a second treatment. This was found to be the case when the same freeze-drying procedure was carried out on an unirradiated solution of adenylic acid containing comparable amounts of hydrogen peroxide. It can be seen (cf. Table 3) that the rate, as well as the amount, of phosphate release is unaffected by freeze-drying and both are thus independent of the amount of hydrogen peroxide present. One must conclude, therefore, that the post-irradiation phosphate is produced directly from a labile compound formed during irradiation.

It has been shown [5,6] that certain phosphate esters containing the grouping $-CH_2{\cdot}O{\cdot}PO(OH)_2$ can be oxidised to the corresponding acyl phosphate $[-CO{\cdot}O{\cdot}PO(OH)_2]$ on irradiation in aqueous solutions containing oxygen. Since this particular grouping occurs in adenosine-5′ phosphate, solutions of this substance which had been irradiated in the presence of oxygen were tested for

[5] Scholes and Weiss, *Nature*, 1954, **173**, 267.
[6] Wilkinson and Williams, *J. Chim. phys.*, 1955, **52**, 600.

the presence of acyl phosphate. A weak Lipmann reaction [7] was found, but this was also observed in irradiated solutions of the 3′-nucleotides. Thus, because of the apparently non-specific nature of this reaction when applied to these compounds, no definite conclusions can be drawn.

Another method for the detection of acyl phosphates is based on the release of inorganic phosphate under suitable conditions. It is known that acetyl phosphate is catalytically decomposed by molybdate,[8] particularly in acid solutions; *e.g.*, its phosphate group is completely split off under the conditions prevailing in the method of phosphate estimation described by Berenblum and Chain.[9] This catalysis, however, is not quite so marked at pH ~4, and, if

FIG. 4.

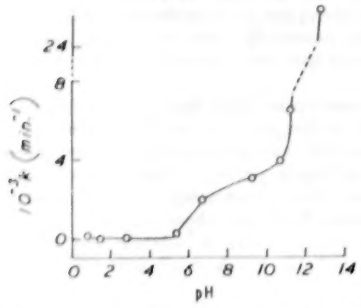
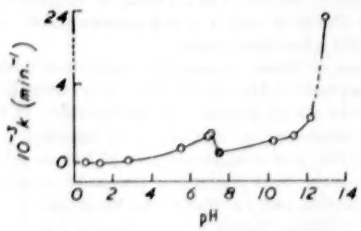


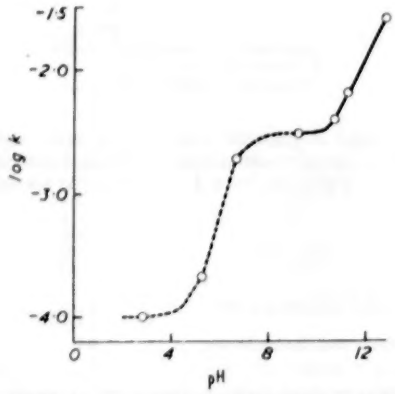

FIG. 5.




FIGS. 4 *and* 5. *Irradiation of aqueous solutions* (0·1% w/v) *of* (*Fig.* 4) *adenosine-3′ phosphate* (*commercial*) *and* (*Fig.* 5) *adenosine-5′ phosphate* (*commercial*) *with* X-*rays* (200 kv) *in the presence of oxygen* (1 *atm.*), *at* pH 6·8—7·0. *Dose* = $8{\cdot}6 \times 10^{-6}$ ev/*N per ml. First-order rate constant* (*k*) *of the post-irradiation phosphate release at* 25° *as a function of* pH.

FIG. 6. *Plot of* log k *against* pH *for post-irradiation phosphate release from adenosine-3′ phosphate* (*commercial*).

○ *Experimental points.*
– – – – *Theoretical curve.*




care is taken, inorganic phosphate can be determined in the presence of acetyl phosphate.[10] If, as seems likely, other acyl phosphates exhibit similar behaviour, this could provide a sensitive test for these compounds. However, in the case of the 5′-nucleotide, it was found that the yields of inorganic phosphate were identical when either Berenblum and Chain's or Lowry and Lopez's method [10] was used; this confirms the absence of any *stable* acyl compound in irradiated adenosine-5′ phosphate solutions. Indeed, it was found that decomposition of the labile 5′-ester was not molybdate-catalysed, either in N-sulphuric acid or at pH 4·1, as was also found to be the case with the labile products from the 3′-nucleotides.

In order to gain some further insight into the nature of the labile compounds the pH-dependence of the rate of hydrolysis was studied. The total amount of inorganic phosphate released

[7] Lipmann and Tuttle, *J. Biol. Chem.*, 1943, **159**, 21.
[8] Weil-Malherbe and Green, *Biochem. J.*, 1951, **49**, 286.
[9] Berenblum and Chain, *ibid.*, 1938, **32**, 295.
[10] Lowry and Lopez, *J. Biol. Chem.*, 1946, **162**, 421.

was constant and followed a first-order law over the whole range of pH in which it was possible to measure it. Figs. 4 and 5 show the variation of the rate of phosphate release with pH in the cases of the irradiated (commercial) adenosine-3′ and -5′ phosphate respectively. In both instances the reaction is strongly base-catalysed and extremely slow in acid solutions. For the 3′-isomer, the behaviour in the region pH 5—9 is rather suggestive of the dissociation of a weak acid and this appears more striking when the logarithm of the rate constant is plotted against pH (Fig. 6). With the 5′-isomer there is a rather striking inflexion in the region pH 7—8 where the rate constant decreases from $1{\cdot}3 \times 10^{-3}$ min.$^{-1}$ at pH 7·0 to $0{\cdot}50 \times 10^{-3}$ min.$^{-1}$ at pH 7·5, thereafter slowly increasing with pH until base-catalysis predominates in the region of pH 12.

At this point it was necessary to consider the fact that the commercial nucleotide-3′ phosphates are actually mixtures of the closely related 2′- and 3′-isomers.[11] *A priori*, there was no reason to expect that only one of the isomers would give rise to labile phosphate on irradiation; to investigate this, some experiments were carried out on pure samples of adenosine-3′ phosphate (isomer *b*) and adenosine-2′ phosphate (isomer *a*). The results obtained (Table 4) show the somewhat surprising fact that, under otherwise identical experimental

TABLE 4. *Irradiation of aqueous solutions* (0·1% *w/v*) *of ribonucleotides with* X-*rays* (200 kv) *in the presence of oxygen* (1 *atm.*) *at* pH 6·8—7·0. *Dose* $= 8{\cdot}67 \times 10^{-6}$ ev/*N per ml.*

| Nucleotide | Inorganic phosphate ($10^{-8}$ mole/ml.) | "Labile phosphate" (*i.e.*, post-irradiation release of inorganic phosphate) ($10^{-8}$ mole/ml.) | $10^{-3}k$ (min.$^{-1}$) at pH 6·75 and at 25° |
|---|---|---|---|
| Adenosine-2′ phosphate (isomer *a*) ... | 1·9 | 0·65 | ~10 |
| Adenosine-3′ phosphate (isomer *b*) ... | 2·60 | 5·2 | 1·7 |

conditions, eight times as much labile phosphate is obtained from the 3′- as from the 2′-isomer. The release of phosphate from the 3′-phosphate fits a first-order plot and that from the 2′-ester does so approximately, although in the latter case it was difficult to make very accurate measurements because of the rather small amounts of phosphate released. At 25° and pH 7, the rate constant ($k$) of phosphate release from the 3′-isomer ($1{\cdot}7 \times 10^{-3}$ min.$^{-1}$) is almost identical with that observed for the mixture at the same pH ($1{\cdot}85 \times 10^{-3}$ min.$^{-1}$) whilst that for the 2′-isomer is about six times greater ($\sim 1{\cdot}0 \times 10^{-3}$ min.$^{-1}$). If it is assumed [11] that the commercial specimen is a 3 : 2 (w/w) mixture of 3′- and 2′-nucleotide and that the radiation-induced attack is divided between these two compounds solely according to their proportions, the yields obtained from the mixture can be accounted for. Further, in view of the small amounts (both relative and absolute) of labile phosphate formed from the 2′-isomer and also because of the greater rate of hydrolysis of this material, it seems legitimate to assume that in the irradiation of the commercial 3′-nucleotide the measured rate of hydrolysis is that of the labile ester from the 3′-isomer.

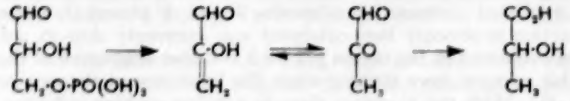
The rate of release of phosphate from irradiated solutions of adenosine-3′ phosphate (commercial) has also been studied as a function of temperature. After irradiation, the solutions were hydrolysed at 15°, 25° and 35° and separate runs were carried out at pH 8·5 and 11·2. In all cases, inorganic phosphate was released according to a first-order law and, as expected, log $k$ was a linear function of $1/T$. This gives a value of 26·3 kcal./mole for the overall activation energy of hydrolysis at pH 8·5 and of 26·6 kcal./mole at pH 11·2.

## DISCUSSION

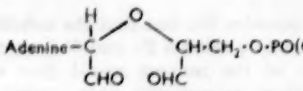
In a consideration of the chemical nature of the labile phosphate esters produced on irradiation, the observed lability towards alkali appears to be of special significance. Fleury *et al.*[12] have investigated the pH-dependence of the hydrolysis of a wide variety of phosphate esters and pointed out that alkali-lability (but only slight acid-lability) is characteristic of esters containing a free carbonyl group. In addition, it is well known that phosphate esters of β-keto- and β-aldehydo-alcohols, *e.g.*, 3-glyceraldehyde 1-phosphate, readily lose their phosphate on treatment with alkali; [13] lability in the latter case

[11] Carter and Cohn, *Fed. Proc.*, 1948, **8**, 190; Khym and Cohn, *J. Amer. Chem. Soc.*, 1954, **76**, 1818.
[12] Fleury, Courtecis, and Desjobert, *Bull. Soc. chim. France*, 1948, **15**, 694.
[13] Meyerhof and Lohmann, *Biochem. Z.*, 1934, **271**, 89.

is probably associated with a β-elimination [14] rather than with a normal hydrolytic process, *viz.*:



This suggests that the radiation-induced lability of the nucleotides is due to the formation of activating carbonyl groups in the sugar components. In this respect, some experiments



(I)

by Brown, Fried, and Todd [15] on the periodate oxidation of adenosine-5′ phosphate are of interest. This reagent oxidises the nucleotide to a dialdehyde of the structure (I) in which the phosphate group is in β-position to the activating carbonyl (formyl) group; these authors found that the phosphate could be removed in mildly alkaline solution at room temperature, a lability which is comparable to that of the irradiation products studied here.

It must be pointed out, however, that the alkali-lability of the 3′- and the 5′-nucleotide irradiation products does not necessarily imply that the carbonyl group is always formed in a β-position to the $>CH\cdot O\cdot PO(OH)_2$ or $-CH_2\cdot O\cdot P\cdot O(OH)_2$ group respectively, since, under the alkaline conditions where release of phosphate occurs, the possibility of enolisation cannot be ignored. This may be illustrated as follows: if the initial attack on, for example, adenosine-5′ phosphate leads to a carbonyl group at the 2′-position, the product (II) thus formed may not be expected to be particularly labile. However, if enolisation takes place, this could possibly result in the formation of a 3′-keto-ester (III) which can

(II) (III)

undergo β-elimination as discussed above. Such additional complexities, therefore, make it difficult, on the basis of these experiments alone, to determine the exact position of attack in the sugar moiety.

The variation of the rate constant of phosphate release with pH (Figs. 4 and 6) can be accounted for on the assumption that the rates of hydrolysis of the various ionised forms of the labile phosphate esters are rather different in magnitude.[16] In particular, the variation of the rate in the pH region 5—8 can be attributed to the ionisation of the mononegative to the dinegative form. On this basis and in the case of adenosine-3′ phosphate (commercial), a theoretical curve can be calculated which fits the experimental results. It can be readily shown that, if the two different ions are hydrolysed at different rates (rate constants $k_1$ and $k_2$):

$$R\cdot PO_4H^- + H_2O \xrightarrow{k_1} R\cdot OH + H_2PO_4^- \quad . . . . . (2)$$

$$R\cdot PO_4^{2-} + H_2O \xrightarrow{k_2} R\cdot OH + HPO_4^{2-} \quad . . . . . (3)$$

then

$$k_{exp.} = k_1/\left\{1 + (K_2/[H^+])\right\} + k_2/\left\{1 + ([H^+]/K_2)\right\} \quad . . . . . (4)$$

where $k_{exp.}$ is the experimentally determined rate constant and $K_2$ is the second dissociation constant of the labile phosphate ester. Depending on the relative values of $k_1$, $k_2$, and $K_2$,

[14] Linstead, Owen, and Webb, *J.*, 1953, 1211.
[15] Brown, Fried, and Todd, *J.*, 1955, 2206.
[16] Cf. Bacher and Kauzmann, *J. Amer. Chem. Soc.*, 1952, **74**, 3779.

the experimental rate constant will, at a certain acid pH, be closely approximated by $k_1$ and towards the alkaline region by $k_2$. From Fig. 6 it can be seen that $k_1 \ll 1 \times 10^{-4}$ min.$^{-1}$ and $k_2 = 3{\cdot}02 \times 10^{-3}$ min.$^{-1}$ at 25°. For a given value of $K_2$ both terms on the right-hand side of the equation (4) can be evaluated as a function of pH and $k_{exp.}$ thus calculated. By successive approximation it was found that $pK_2 = 6{\cdot}6 \pm 0{\cdot}05$. In Fig. 6 the experimental points and the theoretical curve are plotted together and these show satisfactory agreement. The $pK_2$ value, which arises from this treatment, is somewhat different from that of adenosine-3′ phosphate (6·0—6·2). It is of interest that the direction of change in $pK_2$ in going from adenylic acid to the labile product is similar to that found in going from glycerol 1-phosphate ($pK_2$ 6·44) to glyceraldehyde 3-phosphate ($pK_2$ 6·75), *i.e.*, for a process involving the conversion of $-CH_2{\cdot}OH$ into $-CHO$. These observations may support the view that the labile ester contains an activating carbonyl group. In the case of adenosine-5′ phosphate (Fig. 5) a behaviour similar to that of the 3′-isomer is observed in the pH range 5—7; however, above this pH (where ionisation to the dinegative form is complete) additional complications set in which tend to obscure the above simple statement. The fall in the rate constant above pH ~7 may perhaps be connected with ring fission in the sugar moiety leading to a product which is hydrolysed more slowly.

Following the primary radiation process [reaction (1)] we may represent the initial oxidation of the nucleotide (RH) by OH radicals as :

$$RH + OH \longrightarrow R\cdot + H_2O \quad \ldots\ldots\ldots\ldots \quad (5)$$

This leads to the organic radical R·.

Dehydrogenation of the nucleotide by hydrogen atoms, *viz.*, $RH + H \longrightarrow R\cdot + H_2$, appears to be inconsistent with the results since this, in general, should lead to rather high yields of hydrogen. *In vacuo*, therefore, the hydrogen atoms must either recombine or, if they do react with the nucleotide, it must be in such a way as not to yield molecular hydrogen. After reaction (5), the organic radicals may undergo oxidation or reduction, *viz.* :

$$R\cdot + OH \longrightarrow ROH \quad \ldots\ldots\ldots\ldots \quad (6)$$

$$R\cdot + H \longrightarrow RH \quad \ldots\ldots\ldots\ldots \quad (7)$$

$$2R\cdot \longrightarrow (R^+ + R^-) \longrightarrow RH + ROH \quad \ldots\ldots\ldots \quad (8)$$

In the presence of dissolved molecular oxygen, hydrogen atoms are converted into $HO_2$ radicals,

$$H + O_2 \longrightarrow HO_2 \quad \ldots\ldots\ldots\ldots \quad (9)$$

and primary dehydrogenation of the nucleotide [reaction (5)] can be followed by the addition of oxygen to form organic peroxy-radicals :

$$R\cdot + O_2 \longrightarrow RO_2\cdot \quad \ldots\ldots\ldots\ldots \quad (10)$$

Thus, under these latter conditions, we have the following possible (overall) reactions :

$$RO_2 + OH \longrightarrow ROH + O_2 \quad \ldots\ldots\ldots\ldots \quad (11)$$

$$RO_2 + RO_2 \longrightarrow RO_2^+ \ldots RO_2^- \quad \ldots\ldots\ldots\ldots \quad (12)$$

$$RO_2 + HO_2 \longrightarrow RO_2^+ \ldots HO_2^- \quad \ldots\ldots\ldots\ldots \quad (13)$$

$$RO_2^+ \ldots RO_2^- + H_2O \longrightarrow ROH + RO_2H + O_2 \quad \ldots\ldots\ldots \quad (14)$$

$$RO_2^+ \ldots HO_2^- + H_2O \longrightarrow ROH + H_2O_2 + O_2 \quad \ldots\ldots\ldots \quad (15)$$

$$HO_2 \rightleftharpoons H^+ + O_2^- \quad \ldots\ldots\ldots\ldots \quad (16)$$

$$RO_2 + O_2^- \longrightarrow RO_2^- + O_2 \quad \ldots\ldots\ldots\ldots \quad (17)$$

$$RO_2^- + H^+ \rightleftharpoons RO_2H \quad \ldots\ldots\ldots\ldots \quad (18)$$

From this scheme, it can be seen that, whatever the detailed mechanism may be, the only effective change in the absence of oxygen is of the type $RH \longrightarrow ROH$, whereas in the presence of oxygen two products may possibly arise, namely, ROH and $RO_2H$.

As regards specific attack on the ribose residue at position 5′ on the one hand, and at position 2′, 3′, and 4′ on the other, the possible products are summarised as in Table 5.

Its interesting feature is that ROH, which is formed in both the presence and the absence of oxygen, leads in all cases to a carbonyl compound and this is in agreement with the experimental finding that the formation of a labile ester does not depend on the presence of oxygen. Since there was no evidence for the presence of hydroperoxides in the irradiated solutions of the purine nucleotides and since that observed in the cytidylic acid solutions is

TABLE 5. *Possible products from the oxidation of the pentose component.*

| Position of attack | Products *via* ROH | Products *via* $RO_2H$ |
|---|---|---|
| 5′-$CH_2$·OH | $-CH(OH)_2 \longrightarrow -CHO$ | $-CH\langle^{OH}_{O_2H} \longrightarrow \{^{-CHO\ or}_{-CO_2H}$ |
| 2′-, 3′-, or 4′- >CH·OH | $>C(OH)_2 \longrightarrow >CO$ | $>C\langle^{OH}_{O_2H} \longrightarrow >CO$ |

probably connected with the base, it seems that any hydroxyhydroperoxides, if formed at all in the pentose components, decompose rather rapidly. Possible modes of decomposition of these compounds are indicated in Table 5.

It seems reasonable to suppose that inorganic phosphate is formed during the irradiation (cf. Figs. 1—3) by direct attack of the radicals on the carbon atom to which the phosphate group is attached, *i.e.*, at position 3′ in the 3′-nucleotides and at 5′ in the 5′-nucleotide. The overall picture here is, however, not quite straightforward. It may be noted, for instance, that the yield of inorganic phosphate *increases* in the absence of oxygen in the case of the purine-3′ nucleotide, but *decreases* in that of the pyrimidine-3′ nucleotide; this seems to indicate a specific effect due to the base. Further, the yield–dose plots of inorganic phosphate from the 3′-nucleotides are non-linear, the $G$(inorganic phosphate) increasing with increasing dose; this suggests that primary radical attack leads to a product which, as its concentration builds up, is then preferentially attacked so that the rate of formation of inorganic phosphate increases.

## EXPERIMENTAL

*Irradiations.*—The source of $X$-rays was a Victor Maximar therapy tube, without filters and operating at 200 kv and 15 mA. The dose-rate was $2{\cdot}7 \times 10^{-7}$ ev/$N$ per ml. per min., as determined by the ferrous sulphate dosimeter ($G_{Fe^{3+}}$ being taken as 15·5).[18] Irradiations were carried out in Pyrex glass vessels as previously described.[19] For experiments in the presence of oxygen the solutions were saturated with the gas. Evacuation was effected by pumping out with a two-stage oil-pump backed by a mercury diffusion pump; by this means it was shown that the pressure of oxygen in equilibrium with the solution did not exceed $10^{-6}$ mm.

Triply distilled water, used in all experiments, was prepared by distilling ordinary distilled water from alkaline permanganate and then from phosphoric acid in a "Baraglass" still of the type described by Smith.[20] The nucleotide solutions were brought to pH 6·5—7·0 by the addition of "AnalaR" sodium hydroxide.

*Freeze-drying.*—The apparatus used was based on a model described by Holtzman.[21] The solution (100 ml.) was frozen in thin layers in four 250 ml. flasks which were then attached to a central flask immersed in solid carbon dioxide–methanol. The whole apparatus was continuously evacuated by an oil-pump until sublimation into the central vessel was complete. A water reservoir was included in the apparatus, so that at the end of the freeze-drying a little water vapour could be condensed on the powder remaining; this prevented losses which were likely to occur on opening of the apparatus to the air.

*Inorganic Phosphate.*—For the estimation of inorganic phosphate in the presence of labile phosphate a slight modification of the method of Berenblum and Chain [9] was employed. To an aliquot part (10 ml.) were added 10N-sulphuric acid (1 ml.), water (4 ml.), 5% (w/v) ammonium molybdate (5 ml.), and butan-2-ol (20 ml.). The whole was shaken for 1 min., the acid aqueous layer run off, and the butanol extract washed with N-sulphuric acid (2 × 10 ml.). The inorganic

[17] Mackinnon and Waters, *J.*, 1953, 323.
[18] Farmer, Rigg, and Weiss, *J.*, 1955, 582.
[19] Farmer, Stein, and Weiss, *J.*, 1949, 3241.
[20] Smith, *Chem. and Ind.*, 1938, **57**, 936.
[21] Holtzman, *Science*, 1950, **3**, 550.

layer was transferred to a second flask (reserved for this stage) where reduction of the phosphomolybdate was accomplished by shaking with a 0·4% (w/v) solution (30 ml.) of stannous chloride in N-sulphuric acid for 30 sec. The blue butanol layer was then made up to 25 ml. with ethanol and the extinction measured in a Spekker colorimeter with a red (Kodak 608) filter. Calibration was with "AnalaR" disodium hydrogen phosphate.

To prevent "false" colours it was necessary to purify the butan-2-ol and ethanol; these were refluxed over calcium hydroxide and sodium hydroxide and then fractionally distilled. To avoid interference by silicomolybdate the molybdate reagent was stored in a polythene bottle. Polythene vessels were used for the hydrolyses, this being particularly essential for alkaline solutions.

Lowry and Lopez's method was used as described by these authors.[10]

*Hydrogen Peroxide.*—This was estimated with titanium sulphate according to Eisenberg's method,[22] with a Spekker colorimeter and blue-violet filter (Kodak 601) and by iodide according to the procedure described by Hochenadel [23] with a "Unicam" spectrophotometer (S.P. 500) (optical density measured at 353 mμ).

*Materials.*—Wherever possible "AnalaR" reagents were used. Commercial preparations of adenosine-3′ phosphate, cytidine-3′ phosphate, and adenosine-5′ phosphate were supplied by Roche Biochemical Products. The samples of the adenylic acid *a* and *b* were obtained from Schwarz Laboratories (New York).

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NEWCASTLE UPON TYNE, 1. [*Received, April 9th*, 1956.]

[22] Eisenberg, *Ind. Eng. Chem., Analyt.*, 1943, **15**, 327.
[23] Hochenadel, *J. Phys. Chem.*, 1952, **56**, 587.

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## 735. *Steric Effects in Electronic Spectra.*

By J. N. MURRELL.

The importance of steric effects in determining the electronic spectrum of a composite molecule is related to the interaction between locally excited and electron-transfer states of the separated fragments. The intensity of a transition to a typical electron-transfer state is in general more sensitive to steric factors than a transition to a typical locally excited state, but the latter is usually more sensitive in its frequency. The electronic spectra of the diphenyls, dimethylanilines, acetophenones, and cyanine dyes are briefly discussed, and the nature of their electronic bands determined from the effect of *ortho*-substituents on their spectra.

IT is well known that when two conjugated fragments R and S are joined by a single bond the electronic spectrum of the molecule depends sensitively on the degree of coplanarity between the two fragments. If R and S lie in mutually perpendicular planes, the spectrum of the molecule RS strongly resembles the superimposed spectra of RH and SH.

In such a molecule, the intensity of an absorption band usually decreases on steric distortion from the coplanar configuration, although in some cases the intensity remains relatively unchanged: in principle it is possible for the intensity to increase, but examples of this are difficult to find. There are many cases, however, in which the frequency of a band either increases or decreases or remains unchanged as the molecule is distorted. The relevant experimental work has been reviewed by Braude and Waight.[1]

Longuet-Higgins and Murrell [2] have shown that the electronic spectrum of a composite molecule can be conveniently described in terms of wave functions for the separated fragments. These functions fall into two classes: those which describe excited states of the individual fragments (locally excited states; denoted L.E. below); and those

[1] Braude and Waight, "Progress in Stereochemistry," Butterworths, London, 1954.
[2] Longuet-Higgins and Murrell, *Proc. Phys. Soc.*, 1955, **68**, *A*, 601.

which describe a state in which an electron has been transferred from one fragment to another (electron-transfer states; denoted E.T. below). Transitions from the ground state to the L.E. states give rise to the band spectra of the individual fragments; transitions to the E.T. states are forbidden when the fragments are separated, and so are not observed.

The effect of conjugation between the fragments will be to mix the E.T. states both with the ground state and with the L.E. states. The L.E. states do not mix either with each other or with the ground state to any large extent, since there is no direct interaction element between them. Now, if the perturbation is small, the wave functions for the separated fragments will retain their general character even in the composite molecule. An exception will be if an L.E. and an E.T. state of the unperturbed system happen to be nearly degenerate: the resulting wave functions of the composite molecule will then be an intimate mixture of the two species.

The electronic bands of RS can therefore be described as having the features of a transition either to an L.E. state or to an E.T. state, or to a mixture of the two. In this paper we shall consider the effect of steric distortion on a transition to a typical L.E. or E.T. state and hence predict the behaviours of a band of intermediate character. By observing the sensitivity of a particular band to steric effects, we should therefore be able to throw light on the nature of the electronic transition involved.

*Theory.*—Suppose the self-consistent molecular orbitals of R are written $\theta_1 \ldots \theta_p$, and those of S are $\omega_1 \ldots \omega_q$, then the ground-state wave function for the system R–S, in which the two fragments are separated by a large distance, can be written as a single antisymmetric function in which the electrons are assigned to the lowest orbitals with paired spins. We are assuming that the molecule has a stable closed-shell ground state.

The L.E. states of R will be some linear combination of singlet configurations of the type, $\theta_k^{-1}\theta_l$, in which an electron has been raised from $\theta_k$ to $\theta_l$: the L.E. states of S will be combinations of the configurations $\omega_m^{-1}\omega_n$. The E.T. states will be made up either of configurations $\theta_k^{-1}\omega_n$ (R→S), or of configurations of the type $\omega_m^{-1}\theta_l$ (S→R).

Now when R and S come together to form the composite molecule, there will be a change in the Hamiltonian, and the states of the unperturbed system will be mixed together. There are three important interactions to be considered: (i) The L.E. states on different fragments will mix under the influence of electron repulsion.[2] (ii) The field or inductive effect of one fragment will mix together the L.E. states on the other fragments;[3] although these interactions lead to significant differences between the spectrum of RS and the spectra of the separated fragments, they are for the most part independent of the degree of planarity in the molecule, and need not be considered further. (iii) Conjugation between the two fragments will mix the E.T. states with the L.E. states and with the ground state. This interaction, since it depends on the resonance integral between $2p\pi$-atomic orbitals on R and on S, will be sensitive to the geometry of the molecule.

By perturbation theory, the first-order approximation to the wave function of a state $\Psi_a$ is given by

$$\Psi_a' = \Psi_a + \sum_r \frac{H_{ar}'}{E_a - E_r}\Psi_r \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $H_{ar}'$ is the matrix element of the perturbation between the states $\Psi_a$ and $\Psi_r$. The second-order approximation to the energy of this state is:

$$E_a' = E_a + \sum_r \frac{(H_{ar}')^2}{E_a - E_r} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

there being no first-order change in energy under the particular perturbation we are considering. Now if $\Psi_a$ is an E.T. state and $\Psi_r$ an L.E. state, the matrix element $H_{ar}'$, being determined by a resonance integral between the two fragments, will be proportional to $\cos\alpha$, where $\alpha$ is the angle between the planes of the two fragments.

[3] Murrell and Longuet-Higgins, *Proc. Phys. Soc.*, 1955, **68** *A*, 329.

The intensity of a transition $\Psi_0' \longrightarrow \Psi_a'$ is given by:

$$M_{0a}' = \int \left( \Psi_0 + \sum_r \frac{H_{0r}'}{E_0 - E_r} \Psi_r \right)^* \varepsilon r \left( \Psi_a + \sum_s \frac{H_{as}'}{E_a - E_s} \Psi_s \right) d\tau \quad . \quad . \quad (3)$$

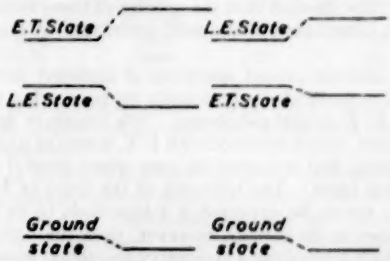
$$= M_{0a} + \sum_{s \neq a} \frac{H_{as}'}{E_a - E_s} M_{0s} + \sum_{r \neq 0} \frac{H_{0r}'}{E_0 - E_r} M_{ra} \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

to the first order in the perturbation. If $\Psi_a$ is the configuration $\theta_p^{-1}\omega_q$, the dipole moment $M_{0a}$ can be reduced to the one-electron integral

$$M_{0a} = \sqrt{2} \int \theta_p \varepsilon r \omega_q d\tau \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and this is small if there is only a small overlap between the orbitals $\theta_p$ and $\omega_q$ on the two fragments. $M_{0s}$ will be large if $\Psi_s$ is an L.E. state, which gives rise to a strong band in the separated fragments. $M_{ra}$ can be non-zero if $\Psi_r$ is an E.T. state in which the electrons are transferred in the same direction as in $\Psi_a$. For a non-zero transition dipole moment between $\theta_p^{-1}\omega_q$ and $\theta_r^{-1}\omega_s$ it is necessary either that $p = r$ or that $q = s$. There are

FIG. 1. FIG. 2.




therefore two main contributions to the intensity of the transition $\Psi_0' \longrightarrow \Psi_a'$. One is due to the presence of L.E. wave functions in the upper state, and the other is due to E.T. wave functions in the ground state. The latter gives rise to an increase in the total intensity of absorption by the molecule. All the terms in eqn. (4) go to zero when the two fragments occupy mutually perpendicular planes; it is therefore evident that transitions to the E.T. states have intensities which are extremely sensitive to steric distortion of the molecule.

If $\Psi_a$ is an L.E. state, then for $H_{as}'$ and $H_{0r}'$ to be non-zero both $\Psi_r$ and $\Psi_s$ must be E.T. states. In this case both $M_{0s}$ and $M_{ra}$ will be small terms, depending on the overlap between molecular orbitals on the two fragments. The main contribution to the intensity of the transition $\Psi_0' \longrightarrow \Psi_a'$ will therefore in general arise from the term $M_{0a}$ in eqn. (4). We therefore expect that transitions to a perturbed L.E. state should have intensities which are relatively insensitive to steric distortion of the molecule. An exception to this will be if the transition $\Psi_0 \longrightarrow \Psi_a$ is symmetry-forbidden. In this case one would expect the second and third terms in eqn. (4) to contribute significantly to the intensity of the band, and this contribution will become zero when the fragments are mutually perpendicular. Second-order terms in the wave functions of the perturbed molecule may also be important in determining the intensity of a weak band.

In general, the more sensitive is the intensity of a band to steric factors, the greater will be the amount of E.T. character in the upper electronic state.

The change in energy of a band due to conjugation between two fragments is more difficult to predict. Consider the cases represented in Figs. 1 and 2. The E.T. state and the ground state repel one another, and so do the E.T. state and the L.E. state. The point which is worth noting is that if the E.T. state lies between the ground state and the

L.E. state, then its energy relative to the ground state might be little changed by conjugation between the two systems (see Fig. 2). If the E.T. state lies very close to the ground state the energy of the E.T. band might in fact be raised. However, if the E.T. state lies above the L.E. state, then the energy of the L.E. band will be lowered by conjugation, since there is no interaction between the L.E. state and the ground state (see Fig. 1). This is a considerable simplification of the problem, but may be a useful guide in deciding the nature of the band.

To summarize: a large hyposochromic shift, on steric distortion of the fully conjugated molecule, suggests that the band arises from a transition to an L.E. state, whilst no shift or a small bathochromic shift suggests that an E.T. state is involved.

If an E.T. state and an L.E. state are degenerate, or nearly degenerate, in the unperturbed system, and if these interact under the influence of the perturbation, then two bands will occur in the spectrum, their separation being of the first order in the resonance integral between the two fragments (proportional to cos $\alpha$).

## Applications

ortho-*Substituted Diphenyls.*—The most fully studied example of the effect of *ortho*-substituents on the spectrum of a benzenoid system is found in the diphenyl series. The interest in these molecules arose from the work of Pickett, Walter, and France [4] on dimesityl and hexachlorodiphenyl. They showed that the spectra of these molecules differed in character from those of diphenyls not substituted in the *ortho*-positions. A selection of the relevant data is shown in Table 1.

Both the bands in the near-ultraviolet spectrum of diphenyl move to shorter wavelengths on *ortho*-substitution; this is particularly noticeable on comparing the frequency of the more intense band in 2 : 2′ and 3 : 3′-dimethyldiphenyl. We therefore deduce that the bands arise from transitions to L.E. states, which interact with E.T. states of higher energy. The intensity of the lower band is uncertain, but it cannot be very great since it does not give a noticeable inflexion to the more intense band. The intensity of the band at 4·98 ev falls appreciably on *ortho*-substitution. This is not to be expected if a transition to an L.E. state is involved. If this interpretation is assumed to be correct, however, then the band would correspond to the 2000 Å band of benzene, which arises from a symmetry-forbidden transition, and has an intensity $\varepsilon$ 7000. Its intensity is therefore expected to be more sensitive to steric effects than that of a band which arises from an allowed transition in the separate fragments.

We therefore suggest that the bands at 4·98 and 4·59 ev in diphenyl arise from transitions to L.E. states. This conclusion is arrived at by other authors, and is borne out by an approximate calculation on the energy of the lowest E.T. configuration. It is found to be about 7·0 ev.

ortho-*Substituted Anilines.*—Substituents in the *ortho*-position to an amino-group are expected to reduce the conjugation between the nitrogen $2p\pi$-orbital and the aromatic ring, since the hydrogen atoms joined to the nitrogen will have difficulty in lying in the plane of the molecule. Klevens and Platt's data [5] for some dimethylanilines are given in Table 2.

Table 1. *The near-ultraviolet absorption of diphenyls.*

| Derivative | Energy (ev) | $\varepsilon_{max.}$ | Energy (ev) | $\varepsilon_{max.}$ |
|---|---|---|---|---|
| Unsubst. | (4·59) [d] | — | 4·98 [a] | 17,000 |
| 2-Me [a] | — | — | 5·27 | 10,500 |
| 2-Bu$^{s}$ [a] | — | — | 5·32 | 10,500 |
| 2 : 2′-$Me_2$ [b] | 4·70 | 800 | 5·46 [a] | (6800) |
| 3 : 3′-$Me_2$ [c] | — | — | 4·86 | 16,500 |
| 2 : 4 : 6 : 2′ : 4′ : 6′-$Me_6$ [d] | 4·69 | 500 | >5·46 | — |

[a] Inflection. [b] Braude and Forbes, *J.*, 1955, 3776. [c] Beavan, Hall, Lesslie, Turner, and Bird, *J.*, 1954, 131. [d] Williamson and Rodebush, *J. Amer. Chem. Soc.*, 1941, **63**, 3018. [d] The lowest band in diphenyl is masked by the more intense band at 4·98 ev; its energy has been estimated by Wenzel (*J. Chem. Phys.*, 1953, **21**, 403) by comparison with related molecules.

They show that amino-substituents introduce a new band into the spectrum; this is to be expected if there is a low-energy E.T. state. We infer that this state gives rise to the band at 4·96 ev, since one *ortho*-substituent does not change the energy of this band appreciably, yet

[4] Pickett, Walter, and France, *J. Amer. Chem. Soc.*, 1936, **58**, 2296.
[5] Klevens and Platt, *ibid.*, 1949, **71**, 1714.

its intensity is halved. Two *ortho*-substituents remove the band from the spectrum altogether. The band at 6·2 ev has an intensity which behaves in a similar way to that of the intense band of diphenyl. In this case, however, *ortho*-substituents produce a shift to longer wavelengths. This is to be expected if there is an E.T. state at lower energies. The bands at 7·04 and 4·09 ev both show the characteristics of transitions to L.E. states; they are repelled by E.T. states

TABLE 2. *The effect of* ortho-*substituents on the spectrum of dimethylaniline* ($f$ = oscillator strength).

| | *NN*-Dimethylaniline | | | | 2 : 6 : *N* : *N*-Tetramethylaniline | | | |
|---|---|---|---|---|---|---|---|---|
| $\nu$ (ev) ..... | 7·04 | 6·21 | 4·96 | 4·09 | $\nu$ (ev) ..... | 6·76 | 5·88 | 4·79 |
| $f$ ..... | 0·79 | 0·54 | 0·28 | 0·04 | $f$ ..... | 0·66 | 0·15 | 0·05 |
| | *NN*-Dimethyl-*o*-toluidine | | | | Benzene | | | |
| $\nu$ (ev) ..... | 6·70 | 5·95 | 5·01 | — | $\nu$ (ev) ..... | 6·74 | 6·14 | 4·88 |
| $f$ ..... | 0·69 | 0·23 | 0·12 | 0·02 | $f$ ..... | 0·69 | 0·10 | 0·0014 |

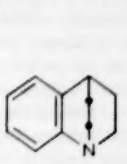
TABLE 3. *Ultraviolet absorption of alkylated acetophenones.*

| | *K*-Band | | *B*-Band | | *R*-Band | |
|---|---|---|---|---|---|---|
| Derivative | $\nu$ (ev) | $\varepsilon_{max.}$ | $\nu$ (ev) | $\varepsilon_{max.}$ | $\nu$ (ev) | $\varepsilon_{max.}$ |
| Unsubst. ..... | 5·10 | 13,200 | 4·44 | 1200 | 3·94 | 55 |
| 2-Me ..... | 5·12 | 8700 | — | — | — | — |
| | 5·06 | 8300 | 4·41 | 1200 | 3·75 | 50 |
| 4-Me ..... | 4·92 | 15,100 | — | — | — | — |
| 2 : 6-Me$_2$ ..... | 4·94 | 5600 | 4·41 | 890 | — | — |
| | 4·84 | 5200 | 4·28 | 740 | — | — |

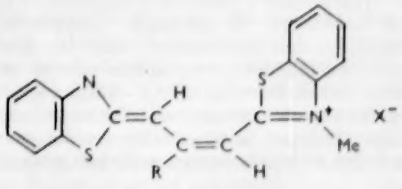
which lie between them. A simple calculation [6] shows that there are two low-energy E.T. states at 6·2 and 5·0 ev. The former will give rise to a rather weak band which would be masked by other transitions in this region.

An interesting example of hindered mesomerism in an aromatic amine is found in "benzoquinuclidine" (I), whose spectrum [7] closely resembles that of benzene.

*Alkylated Acetophenones.*—Unlike benzaldehyde, the spectrum of acetophenone shows noticeable changes when *ortho*-substituents are introduced, evidently owing to steric repulsion between the methyl group of the ketone and the *ortho*-substituent. Table 3 contains some results given by Braude and Sondheimer.[8] There appears to be a balance between the bathochromic shift due to a methyl substituent, and the steric effect. This is best seen by comparing the spectra of 2- and 4-methylacetophenone. The *B*-band resembles the weak band in benzene, and the R-band presumably arises from a $\sigma \longrightarrow \pi$ transition of the carbonyl group; both are little affected by conjugation between the fragments. The *K*-band, however, is considerably reduced in intensity by *ortho*-substituents whilst remaining at about the same frequency. It is therefore assigned to a transition to an E.T. state in which an electron would be transferred from the phenyl to the carbonyl group.




(I)




(II)

*Cyanine Dyes.*—The cyanine dyes are typical of a large class in which there are two conjugated fragments joined by a polyene chain of one, three, or five carbon atoms. As an example of steric effects on the spectra of these molecules, we shall briefly consider the cyanine dye (II). The intense band around 5500 Å is assigned to a transition to an E.T. state. When a substituent R is introduced into the molecule which might be expected to influence its geometry, the

[6] Murrell, *Proc. Phys. Soc.*, 1955, **68**, *A*, 969.
[7] Wepster, *Rec. Trav. chim.*, 1952, **71**, 1159.
[8] Braude and Sondheimer, *J.*, 1955, 3754.

intensity of this band falls considerably. At the same time, however, there is a considerable shift to longer wavelengths. The latter fact can be explained by a strong interaction between the E.T. state and the ground state, which occurs when the two fragments are conjugated together. These two states will repel one another and give rise to a band at shorter wavelengths than that found when there is no conjugation (see Table 4).

TABLE 4. *The absorption spectra of cyanine dyes.*[9]

| R | H | Me | Et | Pr$^i$ | Bu$^n$ |
|---|---|---|---|---|---|
| $\lambda$ ..... | 5550 | 5380 | 5425 | 5450 | 5875 |
| $10^3\varepsilon$ ..... | 149 | 122 | 118 | 94 | 21 |

## DISCUSSION

We have attempted to elucidate the nature of the electronic transitions in the spectra of some composite molecules, from the effects of *ortho*-substitution. Although we have tended to assign a band to a transition either to an E.T. state or to an L.E. state, it must be remembered that this only describes the most important contribution to the wave function of the upper state. In particular, the bands at 4·98 ev in diphenyl and at 6·21 ev in dimethylaniline, although assigned to L.E. transitions, almost certainly have a significant amount of E.T. character. In the same way the band at 4·96 ev in dimethylaniline although predominantly arising from a transition to an E.T. state will perhaps have up to 20% of L.E. character.

There are obviously a great many systems in which *ortho*-substitution will give valuable information about the electronic structure of the molecule, *e.g.*, of nitro-compounds, aromatic acids, and azo-dyes.

I thank Dr. L. E. Orgel for reading the manuscript of this paper and for helpful criticism.

DEPARTMENT OF THEORETICAL CHEMISTRY,
UNIVERSITY OF CAMBRIDGE. [*Received, April 9th*, 1956.]

[9] Brooker, White, Heseltine, Keyes, Dent, and van Lare, *J. Phot. Sci.*, 1953, **1**, 173.

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# 736. *The Preparation of Uniformly* $^{14}$C-*Labelled Substances on a Laboratory Scale, with Special Reference to* L-*Tryptophan.*

By C. E. DALGLIESH and R. W. DUTTON.

A comparison is reported of two methods of biosynthesis, on a laboratory scale, of substances uniformly labelled with $^{14}$C. A two-stage "heterotrophic" approach used biosynthesis of carbohydrate by tobacco leaves and subsequent growth of the food yeast, *Torulopsis utilis*, on labelled substrate. This method is potentially adaptable to preparation of a wide range of labelled substances. A one-stage "autotrophic" approach, suitable for the commoner cell constituents, used the green alga, *Chlorella vulgaris*. Uniformly $^{14}$C-labelled L-tryptophan can be obtained in an overall yield (based on initial $Ba^{14}CO_3$) of 0·2—0·3% by either route. Improved procedures are reported for many of the steps involved. "Infinite thinness" counting was found most suitable for determining, without wastage, the radioactivity of highly active materials available in only limited amount.

THE complexity and stereochemical specificity of many substances required for metabolic investigations make the chemical synthesis of isotopically labelled specimens time-consuming or impracticable, and biological synthesis becomes the method of choice. We have therefore investigated methods of biological synthesis suitable for equipment in a small laboratory.

Only in rare cases can biological synthesis from simple labelled precursors lead to a complex molecule labelled in a specific and predictable position. The choice therefore lies between uniform labelling, the uniformity being ensured as far as possible by requiring all carbon atoms to be derived from a single simple labelled source (preferably $^{14}CO_2$), and

random labelling, *i.e.*, multiple labelling without uniformity. Random labelling is often easier to achieve, *e.g.*, by allowing an organism to incorporate a labelled precursor whilst using another unlabelled substrate as major energy source, but the substances produced are of far less value for metabolic investigations, and we have rejected this approach. Uniformly labelled substances can be obtained with high specific activities, their use makes the results of metabolic experiments much easier to interpret, and moreover all reactions which the substances undergo become theoretically detectable.

Micro-organisms are potentially the most useful agents for preparative laboratory biosyntheses. Two approaches are available. An autotrophic organism can be grown with $^{14}CO_2$ as sole carbon source. This approach is useful for the more universal tissue constituents such as amino-acids, but has the disadvantage that the growth of most suitable autotrophs is slow. Alternatively a heterotrophic organism can be grown on a uniformly labelled substrate (conveniently glucose). This approach has the disadvantages that an additional step is involved in preparing the labelled substrate, and that a proportion of this substrate is lost by respiration (though this respired activity is recoverable without appreciable dilution). It has the advantages that more rapidly growing organisms can be used and that the range of substances potentially obtainable is greatly extended, as it becomes possible to grow a wide range of wild-type or mutant organisms producing different substances in unusual amount. We have used both approaches, and have compared their relative merits for the preparation of uniformly $^{14}$C-labelled L-tryptophan, a substance conveniently prepared by either route and not previously available. The results are, however, much more widely applicable.

Three problems are involved: (1) the growth of a suitable biological system using, as ultimate source of all carbon, $^{14}CO_2$ from the commercially available barium [$^{14}$C]carbonate; (2) the isolation of the required substance; and (3) measurement, without wastage, of the activities of materials of high specific activity available in only small amounts. We have studied the first and third aspects and have confined ourselves largely to published procedures for isolation. For the two-stage "heterotrophic" approach we used tobacco leaves for the photosynthesis of labelled carbohydrate from $^{14}CO_2$ in the apparatus described in the accompanying paper.[1] This carbohydrate was then used as sole carbon substrate for growth of the food yeast *Torulopsis utilis*. For the direct "autotrophic" approach we have grown the alga *Chlorella vulgaris* on $^{14}CO_2$ in the same photosynthesis apparatus.

## Determination of activities

The high activities, and small quantities, of metabolites available severely limit the methods for activity determination. Counting of samples at infinite thickness with standard geometry is inapplicable except after dilution with unlabelled substance, and this involves loss of both time and material. We have therefore investigated other techniques, and compared the values obtained with those derived from "infinite thickness" counting of diluted samples. Of the available methods, gas counting was considered too laborious, as well as requiring a high dilution of samples of the activities encountered. Scintillation counting of samples co-dissolved with a phosphor, and gas-flow counting of solutions, seemed of too limited application. Estimation of *Bremstrahlung* should be speedy and accurate, but with the counters available the activities were insufficiently high. Thus, when a "Coronet" counter [2] was used count rates of only 200 counts min.$^{-1}$ mc$^{-1}$ were obtained, but we consider this might be developed into a suitable method by using other types of counter. We have therefore relied principally on "infinite thinness" counting though, as shown below, this has limitations.

## Experimental

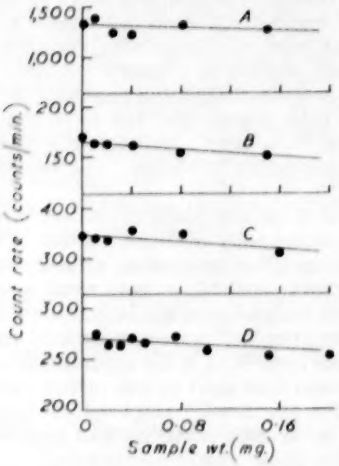
*Apparatus.*—Activities were determined in a counter with a thin mica end-window. Counts were taken for times sufficient to give a standard error of count better than $\pm 3\%$, and in most cases of $\pm 1\%$. All figures quoted are corrected for background and coincidence.

[1] Dutton and Dalgliesh, following paper.
[2] Veal and Baptista, *Brit. J. Radiol.*, 1954, **27**, 198.

Barium [$^{14}$C]carbonate, supplied by the Radiochemical Centre, Amersham, was taken as the ultimate standard, and the figures for activity supplied with the samples were accepted as correct. A standard 1 sq. cm. disc of poly([$^{14}$C]methyl methylacrylate) was used as substandard, and was accurately calibrated in terms of barium [$^{14}$C]carbonate.

*Back-scattering Factors.*—To relate the activities of organic substances to barium carbonate the relative back-scattering factors must be known. Yankwich and Weigl[3] found, for 12% geometry, that the back-scattering factors for air, barium carbonate, and paper or wax, were respectively 1·00, 1·30 ± 0·01, and 1·04 ± 0·015. On the assumption that the factor for paper and wax can be generally applied to organic materials the ratio of back-scattering factors for barium carbonate and organic substances should be 1·25. Yankwich and Weigl's figures are not universally accepted[4] and we considered it desirable to make our own determination.

An annular mount was constructed which fitted closely over a standard 2 sq. cm. Polythene planchette. A thin film of " Formvar " was then spread on a glass slide, floated off in water on to the mount, and dried. A sample of active barium carbonate on a 2 sq. cm. planchette




*The variation of count rate with sample weight for (A) leucine, (B) arginine, (C) phenylalanine, and (D) glucose. The samples for each substance contain a constant activity in a variable weight of material.*

was then counted with and without the mount and film in position. The values obtained were 13,184 ± 115 and 13,466 ± 116 counts/min. respectively. The small difference of the two means indicated that the film was sufficiently thin. Glucose of specific activity 10 μc/mg. was dissolved in water, and 0·05 ml. of the solution was applied to the film and allowed to evaporate so as to give 3 mμc in 0·3 μg of material. The work described below shows that such a sample has no appreciable self-absorption. Inactive barium carbonate and inactive glucose were then compacted in the usual way on 2 sq. cm. Polythene planchettes so that the material was flush with the Polythene surface. Each planchette was then counted with the active source in position over it, and 0·5 mm. from the backing. The means of five determinations, made alternately with each backing, were: barium carbonate 1132 ± 16; glucose 909 ± 13 counts/min. The ratio of these is (1·25 ± 0·025) : 1, in agreement with the results of Yankwich and Weigl.

*Measurement of Thin Films.*—In early experiments the material was distributed on lens tissue, but considerable variations of count rate occurred with small variations in thickness. As the specific activities encountered in the present work were high it was decided to try the counting of films so thin as to approach zero thickness. For such a purpose the lens tissue would have to be omitted, and solutions were therefore placed in several small spots on the surface of nickel planchettes, which were then dried in a vacuum-desiccator or in an oven. Several spots were applied to ensure a greater total perimeter should the material dry out mainly at the edge of the spot. Known weights of glucose were then counted and compared with the calculated count, on the assumption that the glucose had been uniformly spread. This showed that sample weights above 0·2 mg. were undesirable. Below 0·1 mg. the activities

[3] Yankwich and Weigl, *Science*, 1948, **107**, 651.
[4] Glascock, " Isotopic Gas Analysis for Biochemists," Academic Press Inc., New York, 1954, p. 3.

did not vary with sample weight by much more than the standard error of the count, and these conditions were used for counting solutions of highly active materials encountered in the present work. In the Figure are shown the variations of count rate with sample weight for four compounds, determined by diluting aliquot parts of solutions of high activity with known weights of unlabelled material. The activity of the undiluted radioactive material is plotted at zero weight. The method allows determination of activity of solutions of materials containing more than 10 mμc/mg. with an overall statistical and sample preparation error of ±5%. This lowest desirable level of specific activity was appreciably lower than that of most samples described in the present work.

### Photosynthetic production of labelled carbohydrate

Of the various plant materials used by previous workers, tobacco leaves [5,6] seemed most suitable. Bean leaves (*Phaseolus vulgaris*: cf. ref. 7) were less satisfactory. Our photosynthesis apparatus [1] was used, which freed the method from dependence on sunlight. As monosaccharide, rather than starch or sucrose, was the desired end-product, published procedures were unnecessarily laborious. After removal of soluble sugars by aqueous or aqueous-ethanolic extraction, starch has previously been isolated by differential sedimentation of homogenates,[7] by dissolution in aqueous potassium hydroxide and reprecipitation with ethanol,[8] by homogenisation of leaf material with water and toluene, followed by differential sedimentation,[6] by gelatinisation, extraction with aqueous calcium chloride, and precipitation as the starch–iodine complex,[5] or by a similar process of extraction with perchloric acid in place of calcium chloride.[9] All these methods were found to be laborious. A much simpler technique is described below. Soluble sugars are extracted with water. The starch in the leaf debris is then simultaneously hydrolysed and extracted by an aqueous enzyme preparation, and hydrolysis of the extract to monosaccharide is completed by dilute mineral acid. Under our conditions 70—80% of the activity of the initial $Ba^{14}CO_3$ was recovered in the final monosaccharide extracts, the mean value for 7 runs being 74%. This overall yield compares well with other published procedures, and the technique is appreciably simpler.

### Experimental

*Plant Material.*—Seed of *Nicotiana virginica*, Burley, was obtained from Messrs. Thompson & Morgan, Ipswich. It was sown in shallow trays, and seedlings were planted out at 2—4 weeks. "National Growmore" fertiliser was applied monthly, or whenever symptoms of nitrogen deficiency became apparent. Plants were grown beside a south-facing window. In winter they were placed above heaters maintaining a temperature of 15—25°, and the period of illumination was artificially extended to 14—16 hr./day. Under these conditions suitable plants could be raised throughout the year, but winter-raised plants tended to give somewhat lower yields of carbohydrate and occasionally failed to take up carbon dioxide at all.

Plants were used when 6—10 weeks old. They were placed in the dark for 24—60 hr. before use, to deplete the leaves of starch. When complete depletion of starch was demonstrable, three recently emerged leaves, 15—25 cm. in length, of young plants were chosen, their surface area measured, and photosynthesis then carried out (cf. ref. 1).

*Isolation of Carbohydrate.*—The leaves were cut into small pieces and transferred to an Atomix blender. The contents of the beakers into which the leaves dipped in the photosynthesis apparatus were added and the volume made up to 80—100 ml. with water. The leaves were homogenised for 5 min., and the homogenate was centrifuged for 30 min. at 3000 r.p.m. The supernatant "aqueous fraction" was decanted, and the debris was washed with 100 ml. of water and recentrifuged. The aqueous fractions were pooled. The debris was transferred, with water, to a 250 ml. beaker, the volume made up to 100 ml., and the suspension boiled for 2 min. to gelatinise the starch and inactivate enzymes. After cooling to 65°, a bacterial amylase (10 mg.) ("Bacterase"; Norman, Evans, & Rais, Ltd., Manchester) was added and the mixture incubated at 70° for 1 hr., during which the starch was converted into dextrins and maltose. The temperature was again raised to 100° for a short period and when cool the mixture was

[5] Putman, Hassid, Krotkov, and Barker, *J. Biol. Chem.*, 1948, **173**, 785.
[6] Porter and Martin, *J. Exp. Bot.*, 1952, **3**, 326.
[7] Livingston and Medes, *J. Gen. Physiol.*, 1947, **31**, 75.
[8] Villee and Hastings, *J. Biol. Chem.*, 1949, **179**, 673.
[9] Nielsen, *Ind. Eng. Chem., Analyt.*, 1943, **15**, 176.

centrifuged at 3000 r.p.m. for 30 min. The supernatant liquid was decanted and the residue submitted to a second enzymic extraction. The final debris was not further worked up. The efficiency of the extraction is illustrated in Table 1, the mean recovery of activity in soluble form being almost 95%.

TABLE 1. *Efficiency of enzymic hydrolysis and extraction of starch. Percentages relate to the total activity in the leaf material after extraction of soluble sugars.*

| | 1st extract | | 2nd extract | | Final debris | |
|---|---|---|---|---|---|---|
| Run | μc | % | μc | % | μc | % |
| 1 | 550 | 88 | 55 | 9 | 18·3 | 3 |
| 2 | 45 | 83 | 4·8 | 9 | 4·5 | 8 |
| 3 | 278 | 86 | 29 | 9 | 16·1 | 5 |
| 4 | 2250 | 84 | 257 | 9 | 220 | 7 |
| 5 | 3460 | 90 | 230 | 6 | 135 | 4 |

The two enzymic extracts were pooled to give a clear yellow solution, which was evaporated under reduced pressure to 100 ml. Concentrated sulphuric acid (1 ml.) was added and the solution refluxed for 1 hr. to complete hydrolysis. A slight excess of barium carbonate was added to the cooled solution, and the precipitated barium sulphate (which carried most of the colour down with it) was removed and washed with boiling distilled water (50 ml.). The solution was concentrated, and subsequently purified as described by Porter and Martin,[8] salts being removed by precipitation with ethanol, and the crude sugar purified by chromatography on a charcoal–celite column and finally desalted on a mixed-bed ion-exchange resin (Amberlite M.B.1).

The original aqueous extract of the leaf homogenate was similarly submitted to acid hydrolysis before purification, as the reducing-sugar content was found to rise after such treatment.

In most cases the purified de-ionised monosaccharide solutions were used directly when preparing medium for the subsequent stage. Adequate purity was confirmed by paper chromatography and autoradiography. It was not thought necessary rigorously to purify the product, which would involve a considerable loss of yield without compensatory advantage.[10]

Uniformity of labelling in the product was assumed on the basis of the work of, *e.g.*, Gibbs [11] and Vittorio, Krotkov, and Reed.[12]

### CONVERSION OF LABELLED CARBOHYDRATE INTO YEAST PROTEIN

Little attention has been paid to the use of heterotrophic organisms for the biosynthesis of a range of $^{14}C$-labelled substances. We have used the food yeast, *Torulopsis utilis*, about which much information has been acquired in other connections. Previously this, or related organisms, have been used for preparing [$^{15}N$]amino-acids [13] and [$^{35}S$]amino-acids,[14] but have been rejected [15] for $^{14}C$-labelling on the grounds of loss of substrate activity as respiratory carbon dioxide. But by suitable choice of growth conditions anaerobic metabolism can be minimised and the loss of activity by respiration reduced to ~30%, this respired activity in any case being recoverable (as $Ba^{14}CO_3$) without appreciable dilution.

Conditions for obtaining maximum yields of yeast protein, based on the carbohydrate used as sole carbon source, were determined. Secondly, a method for hydrolysis of the synthesised protein and the separation of the amino-acids without destruction or racemisation of the tryptophan was worked out. An apparatus was designed for the efficient aeration of the growing yeast cultures, but proved no more satisfactory than very rapid " shake cultures " which were finally used. The effect of sugar-substrate concentration on yield was reinvestigated, as there seemed some conflict in the literature, and the effect of additional nitrogen, trace elements, and growth factors was also studied. From a number of enzyme preparations tried, pancreatin was selected for hydrolysis of yeast protein. The results of three syntheses are summarised in Table 2.

[10] Udenfriend and Gibbs, *Science*, 1949, **110**, 708.
[11] Gibbs, *Plant Physiol.*, 1951, **26**, 549.
[12] Vittorio, Krotkov, and Reed, *Proc. Soc. Exp. Biol. Med., N.Y.*, 1950, **74**, 775.
[13] Aqvist, *Acta Chem. Scand.*, 1951, **5**, 1031.
[14] Williams and Dawson, *Biochem. J.*, 1952, **52**, 314.
[15] Schieler, McClure, and Dunn, *J. Biol. Chem.*, 1953, **203**, 1039.

TABLE 2. *Distribution of activity in the fractions obtained after yeast syntheses.* (*Expressed as % of radioactivity supplied.*)

| Run : | 1 | 2 | 3 |
|---|---|---|---|
| Activity supplied in $\mu$c : | 820 | 4180 | 4480 |
| Synthesised yeast | 53% | 50% | 54% |
| " Cold TCA extract " | 4 | 4 | 3·5 |
| " Hot TCA extract " | 8 | 8 | 13 |
| Enzymic hydrolysate of protein | 22 | 28 | 27 |
| aliphatic amino-acids | 18·5 | 18 | 21 |
| phenylalanine | — | 0·65 | 0·68 |
| tyrosine | 0·96 | 0·85 | 0·89 |
| tryptophan | 0·25 | 0·20 | 0·50 |
| Recovered $Ba^{14}CO_3$ | 44 | 30 | 29 |

## EXPERIMENTAL

*Materials.*—A culture of *Torulopsis utilis* var. *major* was obtained from Messrs. Barclay, Perkins Ltd., London.

*Apparatus.*—The cultures were grown in 250 ml. conical flasks carrying a B 19 Quickfit joint. Into this socket was inserted a cone carrying an inlet and an exit tube for the slow circulation of air through the flask. Air was drawn through a wash-bottle containing 40% aqueous sodium hydroxide before entering the culture flask and the radioactive carbon dioxide in the respired air was recovered in barium hydroxide traps. The flask was very rapidly shaken in a " microid " laboratory shaker (Griffin & Tatlock, Ltd., London) and the ambient temperature maintained at 30°. The culture medium was as follows: diammonium hydrogen phosphate 0·56 g.; ammonium sulphate 0·47 g.; potassium sulphate 0·29 g.; magnesium sulphate heptahydrate 0·21 g., the whole made up to 1 l. with distilled water and adjusted to pH 4·4 with hydrochloric acid. Ammonia was added to the culture at intervals throughout the growth period to maintain the initial pH. The pH of the medium was followed by using bromocresol-green as internal indicator (0·5 ml. of a 0·2% aqueous solution per 100 ml.). The medium was boiled for 2 minutes before use, which provided adequate sterilisation of the medium with the large innocula used. The growth of the culture was followed by turbidity measurements, calibrated in terms of dry weight, on small aliquot parts removed at intervals. Nitrogen determinations were made by the micro-Kjeldahl method.

The yield and nitrogen content of the yeast were measured in a series of experiments in which the appropriate additions were made to the medium described. The following results were established : (1) The presence of internal indicator had no effect on yield or growth rate (provided it was not added as an alcoholic solution). (2) The yield increased as the sugar concentration was lowered, to reach a maximum when the sugar concentration was 0·5%, below which no further increase was obtained. (3) To obtain this yield at 0·5% sugar concentration the flask must be shaken at or above 1000 cycles/minute. (4) The addition of nitrogen supplements (ammonium sulphate), growth factors (riboflavin, calcium pantothenate, thiamine, pyridoxine, nicotinamide), or trace elements (Zn, Mn, Cu, Na, Mo, and Fe) had no effect on the yield. (5) The addition of synthetic detergent to increase aeration, or the use of an oxygen atmosphere, did not improve the yield.

*Preferred Experimental Procedure.*—A pilot culture, inoculated from agar slope cultures, was grown overnight and harvested in the logarithmic phase of growth. Fresh medium (50 ml.) was inoculated with washed *Torulopsis utilis* from the pilot culture to give an initial dry weight of *ca.* 20 mg. The gas train was started and 10 ml. of a solution containing 2—4 mc in 200—500 mg. of [$^{14}C$]monosaccharide were added portionwise at intervals throughout the growth period to maintain the concentration of monosaccharide at about 0·2%. The addition of sugar, adjustment of pH, and measurement of turbidity necessitated opening the flask with consequent loss of respired carbon dioxide, and were therefore carried out as swiftly as possible.

Growth was followed by turbidity readings, and the culture harvested at the end of the logarithmic phase. The yeast cells were twice washed in distilled water and dried by washing with acetone and then ether. The respiratory $^{14}CO_2$ trapped as $Ba^{14}CO_3$ was recovered in the usual way and stored dry for re-use.

*Fractionation of the* $^{14}C$-*Yeast.*—Acid hydrolysis was unsuitable because of resultant destruction of tryptophan. Alkaline hydrolysis was unsuitable because of the resultant racemisation of amino-acids. Various proteolytic enzyme preparations were therefore examined. The yeast was first extracted with 5% trichloroacetic acid (TCA) solution at room temperature to

give a "cold TCA extract." The yeast was recovered by centrifugation and the process repeated. The acid was removed from the combined extracts by ether extraction, and the aqueous fraction was then freeze-dried and stored. The nucleic acids were removed from the yeast residue in a similar fashion by two extractions with 5% trichloroacetic acid solution at 90° ("hot TCA fraction"); the extracts were similarly treated and stored. The yeast residue was washed twice with acetone and twice with water and then submitted to proteolysis. The criterion of hydrolytic efficiency was the amount of tryptophan found in the supernatant fraction after hydrolysis and centrifugation, expressed as a percentage of that obtained by alkaline hydrolysis. The results are summarised in Table 3. Pancreatin alone was as efficient

TABLE 3. *Yield of tryptophan after various enzymic procedures.*

| Enzyme or enzyme mixture | Yield (% of yield obtained by alkaline hydrolysis) | | Additional yield (%) by alkaline hydrolysis | Total yield (%) |
|---|---|---|---|---|
| Pancreatin (Pancreatin powder U.S.P.XI, Armour Laboratories) | 97, 90, 98 | Mean, 95 | 7 | 104 |
| Pepsin [Pepsin, crystallised pepsin (Porcine mucosa), Armour Laboratories] | 74, 76, 56 | ,, 69 | 31 | 105 |
| Trypsin (Trypsin, B.D.H.) | 69, 77 | ,, 73 | 27·5 | 96·5 |
| Papain (Papainum B.P., Allen & Hanburys Ltd.) | 76, 78, 74 | ,, 76 | 36 | 112 |
| Pepsin and trypsin | 99 | — | 5 | 104 |
| Pepsin, trypsin, and pancreatin | 101 | — | 7 | 108 |
| Papain, pepsin, and trypsin | 118 | — | — | — |
| Pepsin, trypsin, pancreatin, and duodenal mucus (Duodenin, Armour Laboratories) | 115, 110 | ,, 113 | — | — |

The figures for additional yield obtained by alkaline hydrolysis apply only to the first column of figures under the previous heading. Values greater than 100% are due to autolysis, or alkaline hydrolysis, of enzyme protein.

as any of the combinations of enzymes examined. The yeast was suspended in distilled water (100 ml.) and the pH adjusted to 8·2. Pancreatin (25 mg.) and a few drops of toluene were added. The mixture was incubated at 37° for 3 days with frequent shaking and occasional adjustment of pH when necessary. Although 90—100% of the tryptophan was recovered in the soluble fraction after centrifugation, a considerable proportion of this was still peptide-bound. It was found that only 50—60% of the theoretical was recovered in the tryptophan peak after chromatography on a starch column (see below). Thus, making allowance for a column recovery factor, it was calculated that two-thirds of the soluble tryptophan was free and one-third peptide-bound, agreeing with findings later reported by Werner.[16] The supernatant hydrolysate was decanted from the unhydrolysable debris after centrifugation, and evaporated to dryness. It was then taken up in 0·1N-hydrochloric acid (2—3 ml.) and put through a starch column,[17] the aromatic amino-acids being recovered as isolated peaks, detected by following radioactivity and ultraviolet absorption of the eluate. The appropriate fractions were pooled and freeze-dried. The purity of the isolated amino-acids was investigated by chromatography and autoradiography. The tryptophan was generally obtained pure after the one step, but the tyrosine and phenylalanine peaks sometimes contained other amino-acids and required further purification on suitable columns.

### AUTOTROPHIC SYNTHESIS USING *CHLORELLA*

The cultures of *Chlorella* were grown on inorganic media with $^{14}CO_2$ as sole carbon source. It was necessary to maintain rapid growth rates to obtain a product of high protein content. This was carried out as described in the accompanying paper.[1]

TABLE 4. *Typical distribution of activity in the fractions obtained from the* $^{14}$C-Chlorella (*expressed as % of activity supplied*).

| | Run 1 | Run 2 | | Run 1 | Run 2 |
|---|---|---|---|---|---|
| Activity supplied: | 10 mc | 27 mc | Activity supplied: | 10 mc | 27 mc |
| Medium and washings | 2·6 | 0·6 | Ether extracts of TCA extracts | 0·1 | 0·2 |
| Alcohol-ether extract | 20·8 | 16 | Enzymic hydrolysate of protein | 32·5 | 30 |
| "Cold TCA extract" | 9 | 5·9 | aliphatic amino-acids | 24 | 17 |
| "Hot TCA extract" | 10 | 6·2 | tryptophan | 0·26 | 0·33 |

[16] Werner, *Int. Z. Vitaminforsch.*, 1954, **25**, 315.
[17] Moore and Stein, *J. Biol. Chem.*, 1949, **178**, 53.

The $^{14}$C-*Chlorella* obtained was fractionated in a manner similar to that already described for *Torulopsis utilis*, and the aromatic amino-acids were isolated. The activities residing in each of the fractions obtained are summarised, for two high-activity runs, in Table 4.

## Experimental

*Materials.*—A culture of *Chlorella vulgaris* was obtained from Professor Pearsall (University College, London) and maintained on agar slopes. The medium used was essentially that described by Pearsall and Loose,[18] but sodium citrate and glucose were omitted to exclude alternative carbon sources.

*Fractionation of the Synthesised* $^{14}$C-Chlorella.—The *Chlorella* was harvested, washed twice with distilled water by centrifugation, and dried to constant weight at 60°. The dried material was ground under alcohol and continuously extracted (Soxhlet) for 24 hr. with alcohol–ether (4 : 1). The extract was evaporated to dryness and the residue extracted first with cold and then with hot 5% trichloroacetic acid solution, as described for yeast. A comparison of enzymic hydrolyses was made. Pancreatin hydrolysis was again found the most satisfactory and this was used as described above. The hydrolysate was concentrated and the aromatic amino-acids were isolated on starch columns as before.

## Discussion

The immediate aim of these syntheses has been the production of uniformly labelled L-tryptophan. Similar yields were obtained by both the one- and the two-stage syntheses. In the sugar-yeast synthesis 74% of the initial $Ba^{14}CO_3$ activity was converted into monosaccharide suitable as yeast substrate. Of the monosaccharide activity supplied, 19% was recovered as aliphatic amino-acids, 0·7% as phenylalanine, 0·9% as tyrosine, and 0·32% as tryptophan, giving overall yields of 14·5%, 0·5%, 0·7%, and 0·24% respectively. A further 25% of the initial activity was recovered as $Ba^{14}CO_3$ from the respired carbon dioxide, while 7·5% was obtained as crude nucleic acid and 3·1% in the " cold TCA extract." Thus some 28% of the initial $Ba^{14}CO_3$ was converted into useful fractions, or 39% allowing for the activity of the recovered respiratory $^{14}CO_2$.

In the *Chlorella* syntheses some 60% of the activity appeared in useful fractions. The activity contained in the alcohol–ether extract corresponds to the fat content of *Chlorella* grown under these conditions.[19] Although much of the pigment is also removed, some, presumably degraded, material is left which eventually appears in the aliphatic amino-acid fraction. The yield of aliphatic amino-acid was about 20% and of tryptophan 0·3%. The activity in the " cold TCA fraction " was similar to that obtained with *Torulopsis utilis*, but that in the " hot TCA extract " was only half the yeast value, reflecting the much lower nucleic acid content of *Chlorella*.

The yield of total amino-acid and of tryptophan in the case of *Chlorella* was somewhat lower than predicted from the nitrogen content. It is possible that this yield might be raised by an improved hydrolysis. The lower yields resulting from enzymic hydrolysis were, however, accepted as it was necessary neither to destroy nor to racemise the L-tryptophan.

The *Chlorella* syntheses represent a considerable economy of time and effort over the tobacco–yeast syntheses and result in a higher overall amino-acid yield. The *Chlorella* are also a good source of labelled fat. However, the yeast is probably more suitable for the production of labelled nucleic acids and certain vitamins, and analogous use of suitable micro-organisms makes a whole range of substances potentially preparable.

The apparatus and techniques described are considered to be suitable for the economical production of a wide range of uniformly $^{14}$C-labelled compounds on a small scale.

We are greatly indebted to the Medical Research Council for support.

Postgraduate Medical School,
Ducane Road, London, W.12. [*Received, May 9th, 1956.*]

[18] Pearsall and Loose, *Proc. Roy. Soc.*, 1936, *B*, **121**, 451.
[19] Pearsall, *Times Science Review*, Spring, 1954, p. 13.

## 737. *An Apparatus for Preparative Photosynthesis of $^{14}C$-Labelled Substances.*

By R. W. Dutton and C. E. Dalgliesh.

An apparatus is described which permits photo-synthesis on a laboratory preparative scale of systems useful for producing isotopically labelled substances. The biosynthesis of carbohydrate using tobacco leaves and of whole organisms using the alga *Chlorella vulgaris* is illustrated. The system is flexible, depends solely on artificial light, and allows efficient circulation of $^{14}CO_2$ in both gaseous and liquid systems.

In this paper is described an apparatus for the photosynthesis of carbohydrate, using isolated leaves, or for growth of whole organisms using algae. The application of the apparatus is described in the preceding paper. The apparatus makes use of artificial light and is thus independent of weather. Rates of synthesis are comparable with those obtainable by using sunlight.

### Experimental

*Use with isolated leaves.*

*Description.*—The apparatus is designed for the brilliant illumination of tobacco leaves or algae, maintained at a uniform temperature in a continuously circulated atmosphere of air and radioactive carbon dioxide. The carbon dioxide is liberated from $Ba^{14}CO_3$ and provision is made for the recovery of any unassimilated activity. The radioactivity of the circulating atmosphere may be estimated continuously throughout the run.

Fig. 1 illustrates the gas circuit, and Fig. 2 the water-cooling and lighting systems.

For use with isolated leaves only the leaf chamber, *A*, and that portion of the assembly to the right of it in Fig. 1, are used. The chamber, *A*, consists of a 7 l. glass cylinder with ground flanges at each end. The lower end is closed by a removable ground-glass plate held by clamps, the upper end is closed by a desiccator top with a B34 socket. Two wires carrying the mains electricity supply to the pump are sealed into the corresponding B34 cone which also carries an inlet and outlet for the circulating gas and a socket for a thermometer. The pump, *P*, is a small A.C. vibratory model (J. W. Towers, Widnes) primarily designed for the aeration of fish tanks. A Geiger–Müller tube is mounted in a "counting chamber," *B*, the tube being held by four greased rubber rings in the upper half of a bell-shaped black-painted glass chamber. This chamber has a ground flange at the lower end and is sealed by a ground glass plate carrying inlet and outlet tubes. The rubber rings provide an adequate gas seal but allow the Geiger tube to be moved up and down, thus varying the sensitivity of the counting unit. The sensitivity can be further reduced for high-activity work by the application of a coat of cellulose paint to all but the centre portion of the mica window [this paint can be conveniently removed with methyl cellosolve (2-methoxyethanol)]. Water contained in the humid air leaving the leaf chamber is removed from the circulating air stream by the condenser mounted on the inlet side of the counting chamber. If this is omitted condensation occurs on the counter window.

The funnel, *C*, contains lactic acid which may be run on to the $Ba^{14}CO_3$ contained in the liberation chamber, *D*, attached by a spherical ground-glass joint. Traps 1 and 2 of the gas washing unit, between taps $T_5$ and $T_7$, are filled with saturated barium hydroxide solution. Trap 3 contains 40% sodium hydroxide solution. Taps $T_1$—$T_8$ serve to isolate various parts of the apparatus and their use is described below. The gas circuit is completed by the simple manometer, *E*.

The spiral growth chamber, *H*, illustrated in Fig. 1, is only used for photosyntheses with algae. When leaves are used the gas circuit runs directly from leaf chamber to the condenser.

The leaf chamber, *A*, stands in a Perspex cylinder, 25 cm. in diameter (Fig. 2), which serves as a water-jacket. Cooling water enters the lower inlet, *F*, from a constant-head reservoir and leaves to the sink by the upper outlet, *G*. The chamber is warmed by the lighting system, and constant temperatures in the range 20—40° can be maintained by adjusting the height of the constant-level reservoir and thereby altering the rate of flow of cooling water.

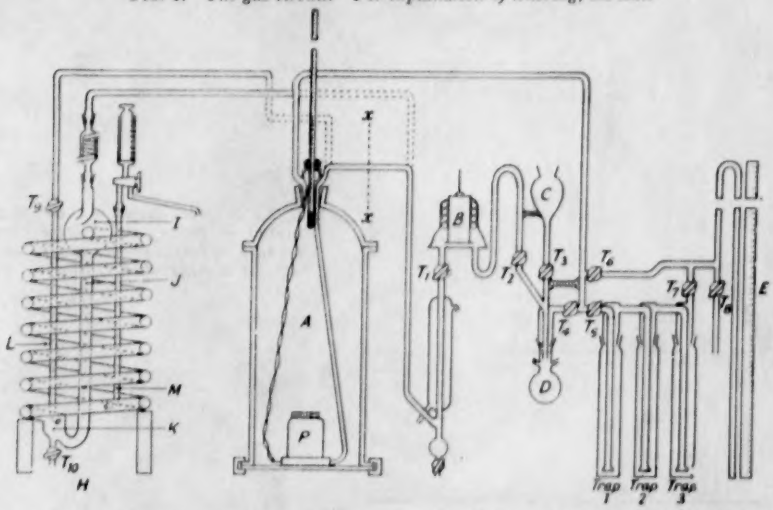
Light is supplied by sixteen 30 w Osram "Striplites," each 28·4 cm. long. Four are mounted on each of four quarter-cylindrical metal reflectors which together form a complete cylinder 40 cm. in diameter. The distance from the lamps to the surface of the leaf chamber is

10 cm. An approximately uniform illumination of about 3000 metre candles in the photosynthesis chamber is thereby obtained. It is necessary to cool the lamps with the fan illustrated (Fig. 2), to prolong their life in the confined space.

*Operation.*—Three or four leaves from a starved tobacco plant [1] are placed in separate 50 ml. beakers on the floor of the leaf chamber. Water (20 ml.) is added to each beaker and a wire frame is inserted to prevent the leaves from falling inwards.

A weighed quantity of $Ba^{14}CO_3$ containing the desired activity is placed in the liberation chamber. The counting chamber and the gas-washing unit are isolated by closing taps $T_1$, $T_2$, and $T_5$, $T_7$ respectively. The three-way tap $T_1$ leaves the counting chamber open to the atmosphere, thus protecting the delicate window should any leak at $T_1$ or $T_2$ develop during the evacuation of the apparatus. The apparatus is then evacuated through $T_8$ to a pressure of about 250 mm. mercury, and $T_8$ is closed. The manometer is read and checked again after 10 min. for leaks. An excess of *ca.* 50% (v/v) lactic acid is then admitted through $T_5$ during 10 min. The spherical ground-glass joint of the liberation chamber allows the contents of the chamber to be agitated should any unwetted $Ba^{14}CO_3$ be deposited on the walls above the level of the acid during the initial effervescence.

FIG. 1. *The gas circuit. For explanation of lettering, see text.*




Complete evolution of carbon dioxide takes about 30 min. Air is then admitted through $T_8$ to a final pressure 100 mm. below atmospheric, then $T_8$ and $T_4$ are closed. After slight expansion of the internal atmosphere when the apparatus is warmed to 30° there is still a slight pressure differential opposing the escape of $^{14}CO_2$ should a leak develop.

Taps $T_1$ and $T_2$ are turned to bring the counting chamber into the gas circuit, and the pump is turned on. The internal atmosphere is thus drawn into the pump and circulated rapidly past the counting chamber, through the liberation chamber, and then back into the top of the leaf chamber. The initial counting rate is measured and the lights are switched on. The circulating activity is measured continuously and readings may be taken at suitable intervals. The lights are turned off when the activity falls to background level. The counting chamber is again isolated and the apparatus evacuated slowly through the gas-washing unit. No precipitate is observed in the barium hydroxide traps after a successful run and this step may thus be omitted if the activity of the circulating atmosphere has fallen to background level. The system is opened to the atmosphere, and the leaves are removed for immediate working up.

*Use with* Chlorella.

*Description.*—The apparatus provides for the adequate illumination, aeration, and agitation of the medium and for the temperature control necessary for the rapid growth of *Chlorella* of high nitrogen content.

[1] Cf. Dalgliesh and Dutton, preceding paper.

The apparatus used for synthesis with tobacco leaves is used in its entirety. The original leaf chamber is now used as a gas reservoir and no longer stands in the illuminated water-bath. This position is instead occupied by the spiral growth chamber, *H* (Fig. 1), which is inserted in the gas circuit between the leaf chamber, *A*, and the counting chamber, *B*. The circuit used in the leaf experiments is broken along the line *x–x*, and the spiral connected into the circuit as shown by the broken lines in Fig. 1. The spiral of the growth chamber has an external diameter of 20 cm. and is 30 cm. high. The internal diameter of the tube is 1·6 cm. and the total capacity 950 ml. The top of the spiral opens into the side of a 250 ml. chamber, *I*. A vertical tube, *J*, leads from the bottom of this chamber to a smaller chamber, *K*, at the lower end of the spiral. The circulating gas is led into this lower chamber by the tube, *L*, and leaves *via* the splash-head mounted in the top of the upper chamber. A small water-cooled condenser is mounted immediately above the outlet. The vertical tube, *M*, opens into the spiral near its base and is surmounted by a detachable 10 ml. syringe which allows a sample to be withdrawn from the spiral *via* a two-way diagonal tap. The spiral growth chamber stands on a Perspex ring and, when it is in position in the bath, the outer surface of the spiral is 10 cm. from the ring of lights. The rest of the apparatus is as described above.

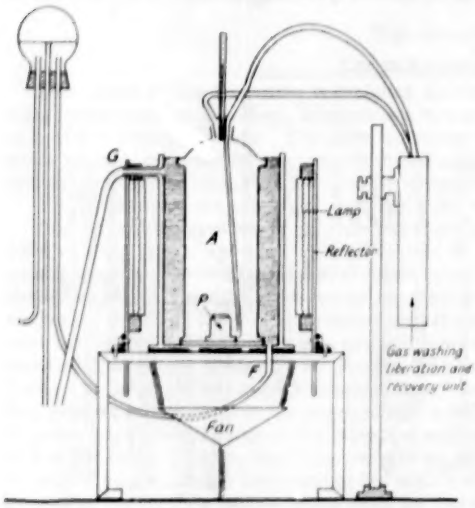



FIG. 2. *A cross-section of the apparatus showing the cooling and lighting systems, in this case the leaf chamber being in the water-bath. For explanation of lettering, see text.*

The circulating gas from the "leaf-chamber" reservoir enters the spiral at the lower chamber, *K*. From here bubbles ascend the length of the spiral, carrying pockets of medium before them. When the upper chamber is reached the gas escapes, to return to the counting chamber *via* the two condensers, while the medium descends again to the lower chamber through the vertical tube, *J*. By means of this "lift-pump" action, the medium is quite rapidly circulated up the spiral and back down the central tube. As the bubbles move up the spiral, the suspension of growing *Chlorella* is flattened out in a thin film around the inside of the tube and considerable local stirring is effected.

*Operation.*—The spiral is partially filled with 650 ml. of medium inoculated with 10—30 mg. of *Chlorella vulgaris*. The operation of the apparatus is much as described for the leaf syntheses. It is necessary, however, to close $T_9$ during the evacuation of the apparatus to prevent the medium from being sucked back through the gas inlet tube. The $^{14}CO_2$ is liberated and the lights are turned on. Samples of the growing *Chlorella* suspension may be withdrawn for turbidimetric or direct dry-weight determinations, by means of the syringe, while the activity in the circulating atmosphere can be measured continuously. The lights are turned off when dry-weight and activity measurements indicate that all the carbon dioxide has been utilised. The uptake of carbon dioxide is virtually quantitative and it is unnecessary to recover residual activity. The spiral is uncoupled and removed from the water-bath, and the dense suspension of *Chlorella* drained from the spiral through the tap $T_{10}$.

## Results and Discussion

*Tobacco Leaves.*—The uptake of carbon dioxide by tobacco leaves is illustrated in Fig. 3, in which the activity in the circulating atmosphere is plotted against time. After a lag period, the rate of uptake becomes linear. The delay before linearity is established is due to two causes: (*a*) the liberation of carbon dioxide and homogenisation of the internal atmosphere is not instantaneous, and (*b*) the internal temperature rises after the lights are switched on, to reach an equilibrium temperature, conveniently about 30°. If the water-bath is initially at 30° and the lights are not switched on until the activity in the circulating atmosphere is constant, the uptake curve is linear from the beginning, but for preparative purposes liberation of carbon dioxide and illumination can be started at or about the same time.

The rate of uptake depends on the condition and the surface area of the leaves over the greater part of the carbon dioxide concentration range used. If these two factors are kept constant, and the number of lights is halved, the rate of uptake is also halved.

Fig. 3. *Uptake of* $CO_2$ *by tobacco leaves.* $^{14}CO_2$ *was liberated from* 1·54 *g. of* $Ba^{14}CO_3$. *Three leaves, of surface area* 780 *sq. cm., together weighing* 26 *g., were used and the mean rate of uptake was* 12·6 *mg. of* $CO_2$ *per dm.*$^2$ *per hr.*

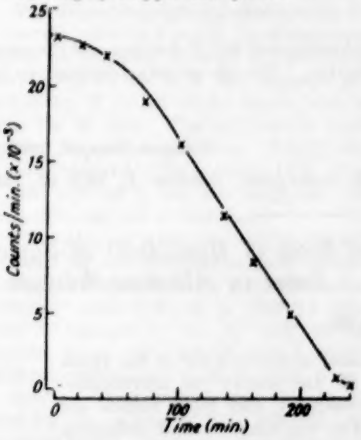
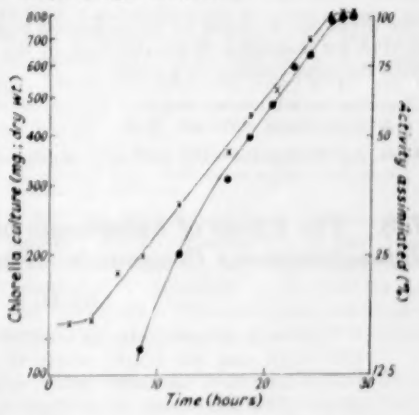



Fig. 4. *Growth of a* Chlorella vulgaris *suspension. The growth curve* (×——×), *and the percentage of circulating* $^{14}CO_2$ *assimilated* (●——●), *are plotted on a logarithmic scale, with* 100% *uptake equated to the maximum dry weight of algae obtained.*




The intensity of illumination is the rate-limiting factor. Under normal working conditions the carbon dioxide content of the circulating atmosphere is initially high (8% if carbon dioxide from 5 g. of barium carbonate is liberated) but although such a concentration would normally be considered toxic it here appears to have no deleterious effect. Similar high initial carbon dioxide concentrations were without toxic effect in the experiments of Putman *et al.*[2] and Porter and Martin.[3] The uptake of carbon dioxide is normally complete, as judged by the absence of precipitate when the internal atmosphere is drawn through the barium hydroxide traps at the end of the experiment. However, leaves from plants raised in mainly artificial light during the winter months were less satisfactory than summer-grown material and occasionally failed to take up carbon dioxide at all.

In a series of seven experiments weights of $Ba^{14}CO_3$ ranging from 1 to 5 g. were used containing up to 9 mc of $^{14}$C. Between 15 and 25 g. (fresh weight) of leaf were used in each run with an average surface area of 700 cm.$^2$. The time taken for assimilation varied from 3 to 7 hr. and the uptake was from 95 to 100%. The rate of uptake of carbon dioxide varied from 8 to 15·4 mg. per dm.$^2$ of leaf area per hour, with a mean value of 12·2.

[2] Putman, Hassid, Krotkov, and Barker, *J. Biol. Chem.*, 1948, **173**, 785.
[3] Porter and Martin, *J. Exp. Bot.*, 1952, **3**, 326.

*Algae.*—The apparatus is designed for the production of algae intended for use as a source of $^{14}$C-amino-acids. The nitrogen content of *Chlorella vulgaris* was found to vary from approximately 4% in resting (agar slope) cultures to 9% in cultures grown at the maximum growth rate. In this work it was therefore necessary to adopt conditions favouring the most rapid rates of growth. This can be achieved by using the spiral growth chamber described. Aeration of the medium is made very simple as the air stream is constrained to flow through the whole medium and for this a small pump is adequate. Further, the whole medium is rapidly circulated and a homogeneous suspension maintained.

The uptake of carbon dioxide, and algal growth, are illustrated in Fig. 4. The growth curve is logarithmic over the greater part of the range, which indicates that neither carbon dioxide concentration nor intensity of illumination is limiting under these conditions, as both these factors alter during the experiment (the effective intensity of illumination falling as the culture density increases). The rate of growth increases with rise in temperature. The apparatus is normally operated at 30°, the mean generation time being 10 hr. In each of a series of experiments the carbon dioxide was liberated from 5 g. of $Ba^{14}CO_3$ containing up to 27 mc. The carbon dioxide uptake was quantitative, and, after being washed and dried, the algae accounted for more than 92% of the carbon supplied. The synthesised *Chlorella* had a mean nitrogen content of 9%.

The two biosyntheses described above are only examples of possible applications of the apparatus, which is both flexible and versatile and is useful in many other problems of preparative photosynthesis.[4]

We thank Mr. A. Ryall for his assistance in glass-blowing and Mr. C. Lordan and the workshop staff for assistance in construction of the apparatus. We are greatly indebted to the Medical Research Council for a grant.

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Ducane Road, London, W.12. [*Received, May 9th*, 1956.]

[4] See, *e.g.*, Badenhuizen and Dutton, *Protoplasma*, 1956, in the press; *Biochem. J.*, 1956, **62**, 13P.

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## 738. *The Effects of Substituents on the Rates of Hydrolysis of Some Organophosphorus Compounds. Part I. Rates in Alkaline Solution.*

By D. F. Heath.

The rates of hydrolysis, in alkaline solution, of compounds of the types RR'P(O)X and RR'P(S)X, where R and R' are alkoxy- or alkylamino-groups and X is an acidic group, are summarized, and more results are given. The mechanism is of type $S_N2$. The electromeric and inductive effects of substituents are usually very similar to those found in carbon chemistry for reactions of this type. However, ethyl *NN*-dimethylphosphoramidocyanidate and compounds containing P–S–C bonding are hydrolysed exceptionally rapidly, perhaps because the cyanide group and the sulphur atom are very readily polarized relatively to the other substituents considered. In the phosphorodiamidic fluoride series, those compounds containing four alkyl substituents are hydrolyzed markedly more slowly than those containing only three, owing to a steric effect. For the same reason diisopropyl phosphorofluoridate is hydrolyzed more slowly than would be expected from its structure.

Organophosphorus compounds of the types RR'P(O)X and RR'P(S)X, where R and R' are alkoxy- or alkylamino-groups and X is an acidic group, are hydrolysed in neutral and alkaline aqueous solutions. Several authors [1,2,3] have discussed the inductive and steric effects of substituents on the rates of hydrolysis of small groups of these compounds. My present purpose is to present more results, and to apply the electronic theory of organic

[1] Topley, *Chem. and Ind.*, 1950, 859.
[2] Ketelaar, Gersmann, and Koopmans, *Rec. Trav. chim.*, 1952, **71**, 1253.
[3] Dostrovsky and Halmann, *J.*, 1953, 503.

chemistry systematically to most of the available data. Rates for reactions catalyzed by hydroxyl ions are discussed in Part I, and rates under conditions where this catalysis can be neglected in Part II.

It is sometimes difficult to assess the reliability of the published constants. The compounds have been studied almost exclusively as biochemical agents, so that accurate constants have not been required. Generally the most recent values have been taken. The effects of substituents are considerable, so that the results are adequate for a semi-quantitative treatment.

## Experimental

*Materials.*—Where rates are taken from other papers no methods for preparation or properties are given.

*NN'*-Di*iso*propylphosphorodiamidic fluoride was prepared by Mr. D. W. J. Lane, of these laboratories. The other compounds were prepared by Mr. D. W. Pound and Mr. J. Hulme of these laboratories. I am indebted to all three for the experimental details and properties given in this section.

*Fluorine Derivatives.*—Ethyl phosphoromorpholidofluoridate was prepared by allowing phosphoromorpholidic dichloride (1 mol.) to react with sodium ethoxide (1 mol.) in toluene. The product was separated by distillation, and let react with 50% aqueous potassium fluoride at room temperature. The product, extracted with chloroform and fractionated, had b. p. 128°/8 mm. The hydroxyl ion consumed on hydrolysis agreed with the formula.

*NN'*-Di*iso*propylphosphorodiamidic fluoride was prepared from [$^{32}$P]phosphorus oxychloride of specific activity 1 mc/g. *iso*Propylamine (42·9 g.) in chloroform (50 ml.) was run into phosphorus oxychloride (28·6 g.) in chloroform (100 ml.) with stirring at −10°. The temperature was allowed to rise to 0°, and aqueous potassium fluoride (29 g. of fluoride, 0·5 g. of potassium carbonate, 29 ml. of water) run in with stirring. The temperature was raised to 40° and held there for 30 min. The chloroform layer was separated and evaporated *in vacuo* until the product began to crystallize. Light petroleum (300 ml.; b. p. 40—60°) was added, and the mixture refluxed. On cooling, 19 g. of product, m. p. 65°, were obtained. Owing to its high specific activity it was not analyzed. Its m. p. agrees with that of samples containing the theoretical amount of nitrogen.

The following were prepared by the method of B.P. 700,322 (analyses by estimation of amine liberated by acid hydrolysis gave theoretical values): *NNN'*-Trimethyl-, b. p. 110°/3 mm., *N'*-ethyl-*NN*-dimethyl-, b. p. 138°/18 mm., *N'*-*n*-butyl-*NN*-dimethyl-, b. p. 101°/1 mm., *NN*-dimethyl-*N'*-*iso*propyl-, b. p. 129°/11 mm., *NN*-diethyl-*N'N'*-dimethyl-, b. p. 102°/10 mm., *NNN'N'*-tetraethyl-, b. p. 128°/22 mm., and *NN*-diethyl-*N'*-methyl-phosphorodiamidic fluoride, b. p. 104—106°/1 mm.; *N'N'*-dimethyl-, b. p. 137°/8 mm., and *N'N'*-diethyl-phosphoramidomorpholidic fluoride, b. p. 153°/8 mm.

*Azides.*—Tetramethyl- and *NN*-dimethyl-*N'*-*iso*propyl-phosphorodiamidic azide were prepared by the method of B.P. 698,093. The compounds cannot be distilled, and were used in the crude state. Determination of the azide liberated by hydrolysis showed purities of 97—98%.

*NN'N''N'''*-Tetra*iso*propylpyrophosphoramide, m. p. 148—149°, was prepared by the method of B.P. 688,766.

*Rates of Reaction.*—(*a*) All rates of reaction in neutral solution and several of the slower ones in alkaline solution were determined on compounds labelled with $^{32}$P. This is the most accurate of the methods used. The hydrolysing medium and the labelled compound were let reach temperature equilibrium (thermostat) and mixed. The hydrolysis products are ions, and not extractable by chloroform. Aliquot parts were extracted from time to time and shaken with an equal volume of chloroform. The layers were separated quickly and counted in a liquid-counting tube. It was sometimes found that 1—2% of the radioactive material remained extractable by chloroform, however long the run. This represents compounds $R_nR'_{3-n}PO$, which are very stable and are often difficult to separate completely from compounds $RR'PO{\cdot}X$ by fractionation or crystallization. This fraction was therefore subtracted from counts of the chloroform layers.

If the unchanged compound has a partition coefficient $K$ for chloroform–water, the fraction unhydrolyzed at time $A/A_0$ is given by:

$$A/A_0 = (1 + 1/K)x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (a)$$

where $x$ is the fraction of the total active material extracted by chloroform.

Two cases must be considered: (i) When the concentration of the compound is negligible compared with that of the hydrolytic agent, the reaction followed first-order kinetics, $A = A_0e^{-kt}$, whence

$$\ln x = -kt - \ln (1 + 1/K) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

If ln x is plotted against $t$, $k$ can be found by the method of least squares.

(ii) When the molar concentration of the compound is an appreciable fraction, say 0·05—0·15, of the concentration of the hydrolytic agent (*e.g.*, if the specific activity of the compound is low), the rate constant can be calculated from the second-order equation:

$$kt(B_0 - 2A_0) = \ln (BA_0/B_0A) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (c)$$

where $B_0$ and $B$ are the hydroxyl-ion concentrations at times 0 and $t$. There does not however appear to be a method for determining the standard error of constants obtained for this equation, so that it is better to set up an equivalent first-order equation as follows: Rewriting eqn. (*c*) we have:

$$t = \frac{1}{k(B_0 - 2A_0)} \cdot \left( \ln \frac{A_0}{A} - \ln \frac{B_0}{B} \right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (d)$$

The corresponding first order equation is:

$$t' = \frac{1}{kB_0} \ln \frac{A_0}{A} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (e)$$

Whence

$$(t - t')/t = \left( \frac{2A_0}{B_0} \ln \frac{A_0}{A} - \ln \frac{B_0}{B} \right) \Big/ \left( \ln \frac{A_0}{A} - \ln \frac{B_0}{B} \right) \quad . \quad . \quad . \quad . \quad . \quad (f)$$

Thus, to find $k$, ln $x$ is plotted against $t$ to afford ln $(1 + 1/K)$ from eqn. (*b*), whence $A$ can be found, and hence $t$ and $t'$. ln $(A/A_0)$ is plotted against $t'$, and $k$ found by eqn. (*e*), the method of least squares being used. The standard error is found in the usual way.

This method is convenient in that $A_0$ need only be known to an accuracy of $\pm 2\%$, which is readily achieved by counting the hydrolyzing solution. There is no need to weigh the organophosphorus compound to determine its concentration in solution by chemical methods, or to find $(B_0 - 2A_0)$ by titration at the end of the reaction.

(*b*) Some rates were determined by estimating consumption of hydroxyl ions by back-titration with standard acid to thymolphthalein. The constants were calculated from eqn. (*c*).

(*c*) The faster rates in alkaline solution (those of some of the fluorides) were determined by a modification of Walker's conductivity method.[4] The cell consisted of two arms at right angles, one containing platinized-platinum electrodes. Standard sodium hydroxide was placed in one arm, and an equal volume of an aqueous solution of the phosphorus compound in the other. The cell was immersed in a thermostat, and, when temperature equilibrium had been reached, partially rotated several times to mix the solutions. The mixture was then drained into the arm containing the electrodes, and the conductivity determined at set times on an a.c. bridge. The conductivity could be read to about $\pm 0{\cdot}1\%$. (The bridge, from Doran Instrument Co. Ltd., Stroud, Gloucestershire, presented no novel features.)

Let $C_0$, $C_t$, and $C_\infty$ be the conductivities at times 0, $t$, and infinity, and let the molar concentration of hydroxyl ions be initially $2a$ times the molar concentration of the phosphorus compounds. Then

$$kt(B_0 - 2A_0) = \ln [C_t + (a - 1)C_0 - aC_\infty] - \ln a(C_t - C_\infty) \quad . \quad . \quad . \quad (g)$$

$(B_0 - 2A_0)$ was found by titrating the excess of hydroxyl ion after reaction for a few minutes in the same proportions as in the run, but at much higher concentrations. $C_0$ was found by the application of eqn. (*f*) to the first few points. $C_\infty$ was found from the values of $C_t$ when more than 90% of the compound had been hydrolyzed by using an approximate hydrolysis constant in eqn. (*g*).

The method was accurate only to about $\pm 3\%$. The mobility of the fluoride ion and other products is such that when $B_0 = 4A_0$ the conductivity is only reduced by about 25% during a run. Also, when the runs lasted more than about 50 min., $C_\infty$ tended to drift slowly to lower values and could not be obtained accurately enough. No cause was found for this. In consequence, however, runs had to be performed rapidly, with some loss of accuracy.

[4] Walker, *Proc. Roy. Soc.*, 1906, *A*, **78**, 157.

*Order of Reactions.*—The rate of disappearance of the organophosphorus compounds followed first-order kinetics within experimental error in all the runs where a large excess of sodium hydroxide was used. Whenever the concentrations of hydroxyl ion and organophosphorus compound were similar, the rate followed second-order kinetics. The rate constants calculated from the second-order equation ($c$) for the hydrolysis of *NN'*-di*iso*propylphosphorodiamidic fluoride are given in Table 1, and are the same throughout the run. The same characteristics are shown by the results already published; the kinetics are of first order with respect to the concentration of both organophosphorus compound and hydroxyl ion.

*Rates of Hydrolysis in Alkaline Solution.*—In Table 2 are given the hydrolysis constants for a series of phosphorodiamidic fluorides, and in Table 3 for a number of other compounds.

## Discussion

The general approach adopted is that reviewed in detail by Hinshelwood, Laidler, and Timms,[5] Hammett,[6] Watson,[7] and Dewar.[8]

Each rate is proportional to the concentrations of hydroxyl ion and organophosphorus compound. The mechanism is thus analogous to the $-S_{E}2$ hydrolysis of many organic esters. Rates should thus be controlled by the ease with which the hydroxyl ion can approach the central phosphorus atom, and by the ease with which the acidic group can be displaced.

As in the hydrolysis of organic esters, the approach of hydroxyl ion depends on the charge on the central atom, on the degree to which the transition state is stabilized by the overlapping of $\pi$-electrons in double bonds in the complex with $p$-electrons in the hydroxyl ion and on steric hindrance by groups surrounding the central atom. The charge on the phosphorus atom in the system AlkO·P:O is affected by the overlap of $p$-electrons on the AlkO-oxygen atom and the electrons in the P:O bond. The effect is to donate electrons to the phosphorus, so increasing its negative charge, *i.e.*, it is a $-E$ effect. The alkyl group donates electrons by an inductive effect ($-I$). In addition, as phosphorus can accommodate more than eight valency electrons,[9,10] both oxygen atoms may be back-co-ordinated to the phosphorus atom, further increasing the net negative charge. Although this is not an electromeric effect in the usual sense, it is likely to depend in a similar way on the relative electronegativities of the central and the attached atoms, so that for the purposes of this paper it will be included as a $-E$ effect. The negative charge on a phosphorus atom is likely to be greater than on a carbon atom with similar substituents, which may lead to greater stability to hydrolysis, and may explain why hexamethylphosphoramide, $(Me_2N)_3PO$, is extremely stable to alkali compared with tetramethylurea, $(Me_2N)_2CO$. The stabilizing influence of electromeric effects on the transition state cannot be allowed for, as nothing is known of the stereochemistry of the transition state. It can only be assumed that the effect is constant. Steric effects may be important, as phosphorus is surrounded by five groups in the transition state.

The ease with which the acidic radical, X, is replaced depends on the strength of the P–X bond in the transition state, and on the readiness with which X accepts a negative charge to separate as an anion, *i.e.*, on the acid strength of XH. There is no need in the compounds under consideration to postulate differences in P–X bond strength, although they are important in the hydrolysis of phosphorus compounds of a different type.[11] Rates of hydrolysis are correlated with the acid strength of XH, but, as the ($E$ + $I$) effects become more positive the stronger the acid, the tendency of X to accept a negative charge in the transition state cannot usually be distinguished from electromeric effects.

*Hydrolysis of Some Fluorophosphorus Compounds.*—The constants for these compounds are given in Table 2. The compounds all contain the group :PO·F, so that we are only concerned with the electronic and steric effects of the alkoxy- and alkylamino-groups.

The $-I$ effect increases up the series, H, Me, Et, Bu$^n$, Pr$^i$. Also, the $-E$ effects of

[5] Hinshelwood, Laidler, and Timms, *J.*, 1938, 848.
[6] Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 96.
[7] Watson, "Modern Theories of Organic Chemistry," Oxford, 1941.
[8] Dewar, "The Electronic Theory of Organic Chemistry," Oxford, 1949.
[9] Phillips, Hunter, and Sutton, *J.*, 1945, 146.
[10] Rothstein, *J.*, 1953, 3991.
[11] Chanley and Feargeson, *J. Amer. Chem. Soc.*, 1955, **77**, 4002.

alkylamino-groups are greater than those of alkoxy-groups, so that we should expect on the electronic theory alone that the rates at any fixed temperature, with some omissions explained later, would decrease and the activation energies increase in the following order (F·PO·F is omitted; the numerals refer to the serial numbers in the Table): $(Pr^iO)_2$ (2), $(Pr^i{\cdot}NH)_2$ (3), $(Me{\cdot}NH)(Me_2N)$ (4), $(Et{\cdot}NH)(Me_2N)$ (5), $(Bu^n{\cdot}NH)(Me_2N)$ (6), $(Pr^i{\cdot}NH)(Me_2N)$ (7), $(Me_2N)_2$ (10), $(Et_2N)(Me_2N)$ (12), $(Et_2N)_2$ (13). This is the order in which the rates

TABLE 1. *Second-order constants determined by the conductivity method for the hydrolysis of* NN′-*diisopropylphosphorodiamidic fluoride in aqueous sodium hydroxide at* 25·08°.* $B_0 = 0{\cdot}00104_2$M, $2A_0 = 0{\cdot}000538$M.

| Time (min.) | Conductivity (arbitrary units) | $k$ (mole min.$^{-1}$) | Time (min.) | Conductivity (arbitrary units) | $k$ (mole min.$^{-1}$) | Time (min.) | Conductivity (arbitrary units) | $k$ (mole min.$^{-1}$) |
|---|---|---|---|---|---|---|---|---|
| 0 | 2530 * † | — | 9 | 2240 | 48·22 | 18 | 2070 | 48·85 |
| 1 | 2484 | 48·81 | 10 | 2214 | 48·90 | 19 | 2056 | 48·81 |
| 2 | 2446 | 49·27 | 11 | 2192 | 49·04 | 20 | 2044 | 48·54 |
| 3 | 2410 | 48·95 | 12 | 2172 | 48·95 | 22 | 2016 | 48·95 |
| 4 | 2377 | 48·90 | 13 | 2152 | 49·09 | 24 | 1995 | 48·63 |
| 5 | 2344 | 49·82 | 14 | 2135 | 48·81 | 26 | 1973 | 48·90 |
| 6 | 2313 | 49·63 | 15 | 2119 | 48·54 | 30 | 1937 | 48·45 |
| 7 | 2287 | 48·95 | 16 | 2100 | 48·90 | 37 | 1885 | 48·45 |
| 8 | 2258 | 49·82 | 17 | 2084 | 48·95 | ∞ | 1672 † | — |

* For brevity only alternate values obtained are given in this table. † Calc.

TABLE 2. *Constants for the hydrolysis in alkaline solution of compounds* RR′PO·F.

| No. | R | R′ | Temp. | $k$ ($OH^-$) (min.$^{-1}$) | $E$ * (kcal. mole$^{-1}$) | Ref.† |
|---|---|---|---|---|---|---|
| 1 | $CH_2{:}CH{\cdot}CH_2{\cdot}NH$ | $CH_2{:}CH{\cdot}CH_2{\cdot}NH$ | 16° | ~1000 | — | *b* |
| 2 | $Pr^iO$ | $Pr^iO$ | 25·00 | 50 | — | *d* |
| 3 | $Pr^i{\cdot}NH$ | $Pr^i{\cdot}NH$ | 10·4 | 18·4 | 11·2 ± 0·5 | *c* |
| | | | 25·09 | 48·9 | | |
| 4 | $Me{\cdot}NH$ | $Me_2N$ | 25·08 | 17·6 | 11·2 ± 0·5 | *c* |
| | | | 39·55 | 42·4 | | |
| 5 | $Et{\cdot}NH$ | $Me_2N$ | 25·0 | 12·3 | 11·4 ± 0·3 | *c* |
| | | | 38·9 | 29·5 | | |
| | | | 42·15 | 35·3 | | |
| | | | 42·2 | 35·1 | | |
| 6 | $Bu^n{\cdot}NH$ | $Me_2N$ | 25·0 | 11·1 | 11·4 ± 0·5 | *c* |
| | | | 25·08 | 10·6 | | |
| | | | 39·55 | 26·1 | | |
| | | | 42·1 | 31·1 | | |
| 7 | $Pr^i{\cdot}NH$ | $Me_2N$ | 25·0 | 8·43 | 11·9 ± 0·5 | *c* |
| | | | 25·05 | 8·05 | | |
| | | | 38·9 | 20·0 | | |
| 8 | $Me{\cdot}NH$ | $Et_2N$ | 25·00 | 1·69 | — | *c* |
| 9 | $O{<}[CH_2{\cdot}CH_2]_2{>}N$ | $Me_2N$ | 25·00 | $9{\cdot}0 \pm 0{\cdot}2 \times 10^{-4}$ | — | *ai* |
| 10 | $Me_2N$ | $Me_2N$ | 28·9 | $4{\cdot}70 \times 10^{-3}$ | 14·7 ± 0·5 | *e* |
| | | | 42·3 | $1{\cdot}32 \times 10^{-2}$ | | |
| 11 | $O{<}[CH_2{\cdot}CH_2]_2{>}N$ | $Et_2N$ | 25·0 | $1{\cdot}0 \pm 0{\cdot}05 \times 10^{-3}$ | — | *ai* |
| 12 | $Et_2N$ | $Me_2N$ | 25·00 | $2{\cdot}878 \pm 0{\cdot}017 \times 10^{-4}$ | 16·58 ± 0·02 | *aii* |
| | | | 50·00 | $2{\cdot}497 \pm 0{\cdot}021 \times 10^{-3}$ | | |
| | | | 70·55 | $1{\cdot}171 \pm 0{\cdot}005 \times 10^{-2}$ | | |
| 13 | $Et_2N$ | $Et_2N$ | 25·2 | $2{\cdot}5 \pm 0{\cdot}2 \times 10^{-5}$ | 17·1 ± 1·0 | *ai* |
| | | | 49·2 | $2{\cdot}2 \pm 0{\cdot}1 \times 10^{-4}$ | | |

* $E$ was often calculated from rates at two temperatures only. Bell ("Acid–Base Catalysis," Oxford, 1941) has given the arguments against this. When, however, more than two temperatures have been used, in this and other work, the Arrhenius plots are satisfactory for this type of compound.

† *ai*, *aii*, *b*, and *c* refer to the methods already described. *d*, Kilpatrick and Kilpatrick, *J. Phys. Colloid Chem.*, 1949, **53**, 1371. *e*, Heath and Casapieri, *Trans. Faraday Soc.*, 1951, **47**, 1093.

fall, and, within the considerable experimental error, the order in which the activation energies increase.

That a second effect also operates may be seen most clearly from the effect on the rate and activation energy of successive substitutions of dimethylamino- for *iso*propylamino-groups. Thus substituting one dimethylamino-group for *iso*propylamino in *NN′*-di-*iso*propylphosphorodiamidic fluoride [converting compound (3) into compound (7)] reduces

the rate 6-fold at 25°, and increases the energy of activation by about 0·7 kcal./mole. The second substitution [converting compound (7) into compound (10)] reduces the rate by a factor of 2400 and raises $E$ by 2·8 kcal./mole. From the general rate equation $k = PZ \cdot e^{-E/RT}$, where $Z$ is the collision number and $P$ is the probability factor, it follows that

TABLE 3. *Constants * for the hydrolysis in alkaline solution of compounds* RR'PO·X, *etc.*

| No. | Compound | $k$ ($OH^-$) (min.$^{-1}$) | Temp. | $E$ (kcal. mole$^{-1}$) | Ref † |
|---|---|---|---|---|---|
| 14 | $(EtO)_4P_2O_2$ | 158 | 25° | — | *d* |
| 15 | $(Pr^n{\cdot}NH)_4P_2O_2$ | $1{\cdot}31 \times 10^{-1}$ | 25 | — | *ai* |
| 16 | $(Me_2N)_3(Me{\cdot}NH)P_2O_2$ | $3{\cdot}10 \times 10^{-2}$ | 25 | — | *e* |
| 17 | $(Me_2N)_4P_2O_2$ | $4{\cdot}7 \times 10^{-3}$ | 100 | — | *ai* |
| 18 | $(Me_2N)_3P_2O_2$ | $4{\cdot}8 \times 10^{-3}$ | 25 | — | *b* |
| 19 | $(MeO)_2PS{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | $2{\cdot}3 \times 10^{-1}$ | 25 | 15·45 | 1, *f* |
| 20 | $(EtO)_2PS{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | $5{\cdot}7 \times 10^{-2}$ | 25 | 16·6 | 1, *f*, *g* |
| | | *1·3* × $10^{-2}$ | 25 | *19·2* | |
| 21 | $(Pr^iO)_2PS{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | $3{\cdot}3 \times 10^{-3}$ | 25 | — | 1 |
| 22 | $(MeO)PO(O{\cdot}C_6H_4{\cdot}NO_2$-*p*$)_2$ | *34* | 25 | *13·4* | |
| 23 | $(EtO)PO(OC_6H_4{\cdot}NO_2$-*p*$)_2$ | 4·3 | 25 | — | 1 |
| | | *31* | 25 | *14·3* | |
| 24 | $(MeO)PS(O{\cdot}C_6H_4{\cdot}NO_2$-*p*$)_2$ | *1·35* | 25 | *13·9* | |
| 25 | $(EtO)PS(O{\cdot}C_6H_4{\cdot}NO_2$-*p*$)_2$ | $4 \times 10^{-1}$ | 25 | — | 1 |
| | | *9·7* × $10^{-1}$ | 25 | *12·1* | |
| 26 | $(EtO)_2PO{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | $5{\cdot}2 \times 10^{-1}$ | 25 | — | *g* |
| | | *4·0* × $10^{-1}$ | 25 | *12·4* | |
| 27 | $(EtO)(EtS)PO{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | 800 | 37 | — | *h* |
| 28 | $(EtO)_2PO{\cdot}S{\cdot}C_6H_4{\cdot}NO_2$-*p* | 150 | 37 | — | *h* |
| 29 | $PO(O{\cdot}C_6H_4{\cdot}NO_2$-*p*$)_3$ | *2060* | 25 | *4·1* | |
| 30 | $PS(O{\cdot}C_6H_4{\cdot}NO_2$-*p*$)_3$ | $3{\cdot}3 \times 10^{-2}$ | 25 | — | 1 |
| | | *12·4* | 25 | *5·7* | |
| 31 | $(EtO)_2PO{\cdot}S{\cdot}C_6H_4{\cdot}SO{\cdot}Et$ | 3·33 | 25 | — | *e* |
| 32 | $(EtO)_2PO{\cdot}S{\cdot}C_6H_4{\cdot}SEt$ | $8{\cdot}1 \times 10^{-1}$ | 25 | — | *i* |
| 33 | $(EtO)_2PS{\cdot}O{\cdot}C_6H_4{\cdot}SEt$ | $9{\cdot}2 \times 10^{-2}$ | 25 | — | *i* |
| 34 | $Me_2N{\cdot}PO(CN){\cdot}OEt$ | $6{\cdot}3 \times 10^{0}$ | 25 | — | *j* |
| 35 | $(Me_2N)_3PO{\cdot}N_3$ | $9{\cdot}5 \times 10^{-4}$ | 25 | — | *b* |
| 36 | $(EtO)_3PO$ | $4{\cdot}86 \times 10^{-4}$ | 25 | 16·1 | *h* |

* Values in italics were determined for aqueous acetone solutions by Ketelaar *et al.*[3], and are not therefore strictly comparable with the rest. However, the effect of substituents on the rates is not likely to be very different within this group.

The constants given by Cavalier [8] are heavily weighted by values obtained very near the beginnings and ends of runs. I have taken the values 3·37 hr.$^{-1}$ at 88° and 0·0093 hr.$^{-1}$ at 13° from the middle of the runs.

† *ai* and *b* refer to the methods described in the text. *d*, Ketelaar and Bloksma, *Rec. Trav. chim.*, 1948, **67**, 665. *e*, Health, Park, and Lane, *Phil. Trans.*, 1955, *B*, **239**, 191. *f*, Ketelaar, *Rec. Trav. chim.*, 1950, **69**, 649. *g*, Williams, *Ind. Eng. Chem.*, 1951, **43**, 950. *h*, Aldridge and Davison, *Biochem. J.*, 1952, **52**, 663. *i*, Gardner and Heath, *Analyt. Chem.*, 1953, **25**, 1849. *j*, Larson, *Acta Chem. Scand.*, 1953, **7**, 306. *k*, Cavalier, *Ann. Chim. Phys.*, 1899, **18**, 449.

(as $Z$ is nearly constant in this series), if $P$ is constant, a graph of ln $k$ against $E$ should be a straight line, of slope $1/RT$. This is consistent for the separate series, (*a*) $(Pr^i{\cdot}NH)_2$, $(Me{\cdot}NH)(Me_2N)$, $(Et{\cdot}NH)(Me_2N)$, $(Bu^n{\cdot}NH)(Me_2N)$, and $(Pr^i{\cdot}NH)(Me_2N)$; and (*b*) $(Me_2N)_2$, $(Me_2N)(Et_2N)$, and $(Et_2N)_2$; but the second series requires a value of $P$ less by a factor of about 11 than the first. Thus increasing the number of N–C bonds from 3 to 4 both increases the activation energy more than would be expected from the inductive effects of the additional alkyl substituent, and decreases the probability factor. Such a combination of effects suggests that the approach of the hydroxyl ion to the phosphorus is hindered by a steric factor in the second series. Models of the molecules made with Hartley–Conmar Robinson [12] atomic models tend to confirm this. Those of the tetra-alkyl compounds are very compact and rigid; those of the trialkyl compounds are much looser, and the alkylamino-groups can be rotated freely.

The bulk of the alkyl groups increases as the hydrolysis rate decreases in both series. Following Taft [13] and Reeve *et al.*[14] we must consider the possibility that the difference in rate within each series is also partly due to steric effects. A steric effect should influence

[12] Hartley and Conmar Robinson, *Trans. Faraday Soc.*, 1952, **48**, 847.
[13] Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 3120.
[14] Reeve, McCoffery, and Kaiser, *ibid.*, 1954, **76**, 2280.

both $P$ and $E$, but the effect on $P$ may well be small and $E$ is not known accurately enough to prove $P$ constant. The steric effect of a given group, however, should depend markedly on the size of the surrounding groups. It is shown in Table 4 that the substitution of a

TABLE 4. *Effect of substituting dimethylamino for ethylamino on the rate constants at 25° for three phosphorodiamidic fluorides* $(Et_2N)(R)PO{\cdot}F$.

| R | Me·NH | $Me_2N$ | $Et_2N$ |
|---|---|---|---|
| $k_{Me}/k_{Et}$ ..... | 10·4 | 11·9 | 11·5 |

dimethylamino- for a diethylamino-group alters the rate by a constant factor in pairs of compounds in which the other alkylamino-groups are very different in size. It is therefore most probable that the changes in rate within each series are due primarily to inductive effects, and that steric effects are of little importance.

The inductive effects are not, however, strictly additive. Thus, substituting one methyl for one ethyl group increases the rate by a factor of about 1·4 [pair (4) and (5)], whereas substituting two methyl for two ethyl groups on the same nitrogen atom increases the rate about 11-fold (Table 4) and not by $1{\cdot}4^2$. Audrieth and Toy [15] have pointed out the powerful hydrogen-bonding properties of the dialkylphosphoramido-group, and it is thus possible that the substituent effects of primary and secondary amino-groups are influenced by interaction with the aqueous solvent.

The rates of reaction of the four fluorides not so far considered fit in well with the rest. Substitution of dimethylamino by morpholino [pairs (9) and (10), and (11) and (12)] increases the rate by a factor of 4—5. The morpholino-group is likely to exert the same steric forces as other dialkylamino-groups, but to be more negative owing to the presence of the oxygen atom in the ring. Consequently hydrolysis should be faster than for the corresponding dimethylamino-compounds. The diallylamino-compound (1) is hydrolysed very rapidly owing to the negativity of the allyl group in the transition state. Similarly Cavalier [16] observed that diallyl hydrogen phosphate is hydrolysed in water about 13 times as rapidly as diethyl hydrogen phosphate. The rate of hydrolysis of di*iso*propyl phosphorofluoridate (2) is unexpectedly slow; an alkoxy-group is expected to exert a much smaller $-E$ effect than an alkylamino-group. It is shown in the following paper that several *iso*propyl esters are hydrolyzed slowly, probably owing to steric effects.

*Hydrolysis of the Compounds of Table* 3.—The effects on the rate constants of altering R and R′ are closely parallel to those already discussed. Substitution of ethyl for methyl decreases the rate [pairs (19) and (20), (22) and (23), and (24) and (25)], as does the substitution of *iso*propyl for ethyl [(20) and (21)]. The pyrophosphoric compounds (14)—(17) show both electronic and steric effects. If a reasonable activation energy is assumed for octamethylpyrophosphoramide the rate constant at 25° is about $2 \times 10^{-5}$ $(OH^-)$ min.$^{-1}$. In a symmetrical pyrophosphoric ester or amide the rate with respect to each phosphorus atom is half the rate with respect to the whole molecule, as both phosphorus atoms are equally readily attacked. In an unsymmetrical compound the rate may be almost entirely accounted for by the rate of attack by the hydroxyl ion on the phosphorus atom surrounded by the most electrophilic substituents. Thus, in octamethylpyrophosphoramide (17), the rate constant per phosphorus atom is about $1 \times 10^{-5}$ min.$^{-1}$. In heptamethylpyrophosphoramide $(Me{\cdot}NH)(Me_2N)PO{\cdot}O{\cdot}PO(NMe_2)_2$ (16), the rate is controlled by the attack on the left-hand phosphorus atom, and the constant is $3{\cdot}1 \times 10^{-2}$ min.$^{-1}$. Thus, substituting methylamino for dimethylamino increases the rate about 3100-fold in these compounds, compared with 3740-fold in trimethyl- (4) and tetramethyl-phosphorodiamidic fluoride (10). In the latter pair this large increase was attributed mainly to a steric effect. The constant per phosphorus atom in *NN′N″N‴*-tetra*iso*propylpyrophosphoramide (15) is $6{\cdot}5 \times 10^{-2}$ min.$^{-1}$. Thus the substitution of two *iso*propylamino-groups for one methylamino- and one dimethylamino-group increases the rate relatively little, as in the fluoride series [(3)–(4)]. Tetraethyl pyrophosphate (14) is naturally hydrolysed the most rapidly, as the alkoxy-groups are more electrophilic than the alkylamino-groups and the acid produced by hydrolysis considerably stronger.

[15] Audrieth and Toy, *J. Amer. Chem. Soc.*, 1942, **64**, 1553.
[16] Cavalier, *Ann. Chim. Phys.*, 1899, **18**, 449.

The substitution of P=S for P=O reduces the rate somewhat [(20)–(26)], as might be expected from the lower electronegativity of sulphur than of oxygen.

Substitution of the ethyl group by the more negative *p*-nitrophenyl group greatly accelerates the rate, as shown by the series of compounds (36), (26), (23), (29), for the P=O compounds, and by the series (20), (25), (30) for the P=S compounds. The constants for all but triethyl phosphate were determined in aqueous acetone by Ketelaar *et al.*[2] who discussed the rates in terms of inductive and steric effects. The stated accuracy is ±10%, so that the activation energies may be seriously in error. Consequently only two points are made here. The substitution of the first ethyl group by *p*-nitrophenyl accelerates the rate more than any successive substitution, because the first introduces a more acidic, and consequently more readily replaceable, group, as well as one exerting a smaller $-E$ effect. In this instance it is possible to separate the effects of the acid strength of HX and the negativity of X. Secondly, there is a much greater disagreement in the constants given for tri-*p*-nitrophenyl phosphorothionate (30) by Ketelaar *et al.*[2] and by Topley [1] than can be accounted for by the difference in medium. This compound is very insoluble in water, and it appears possible that the result quoted by Topley was obtained on a suspension.

The general result of increasing the acidity of the replaced group, X, is to increase the rate. Thus triethyl phosphate (30) is hydrolysed much more slowly than any other diethyl phosphate given in the Table. In the series of tetramethylphosphorodiamido-compounds : $(Me_2N)_2PO{\cdot}X$, the rate increases as the p$K$ of HX decreases. Thus the rate constants at 25° and p$K$'s are fluoride (10), $3{\cdot}4 \times 10^{-3}$, 3·6; azide (35), $9{\cdot}5 \times 10^{-4}$, 4·7; and octamethylpyrophosphoramide (17), $1 \times 10^{-5}$, 6·7. Similarly tetraethyl pyrophosphate (14) is hydrolysed about 300 times faster than diethyl *p*-nitrophenyl phosphate (26), the p$K$'s of *OO*-diethylphosphoric acid and *p*-nitrophenol being 1·5 and 7·1; and oxidising *OO*-diethyl *S*-ethylthioethyl phosphorothiolate (32) to the corresponding *S*-ethylsulphinylethyl compound (31) increases the rate by introducing the negative sulphinyl group.

Compounds containing the P–S–C group and ethyl *NN*-dimethylphosphoramidocyanidate are hydrolysed much more rapidly than would be expected by analogy with those already discussed. Thus *OO*-diethyl *S*-ethylthioethyl phosphorothiolate (32) is hydrolysed more rapidly than diethyl *p*-nitrophenyl phosphate (26), although *p*-nitrophenol is a stronger acid than ethylthioethanethiol; and *OO*-diethyl *S*-*p*-nitrothiophenyl phosphorothiolate (28) is hydrolysed at about the same rate per phosphorus atom as tetraethyl pyrophosphate (14), although *OO*-diethylphosphoric acid is a stronger acid than *p*-nitrothiophenol. Similarly, ethyl *NN*-dimethylphosphoramidocyanidate (34) is hydrolysed $10^7$ times faster than diethyl *p*-nitrophenyl phosphate (26), although the dimethylamino-group has more $-E$ character than the ethoxy-group, and hydrogen cyanide, of p$K$ 9·1, is a weaker acid than *p*-nitrophenol, of p$K$ 7·1. Lastly, *OS*-diethyl *O*-*p*-nitrophenyl phosphorothiolate (27) is hydrolysed about 1600 times faster than diethyl *p*-nitrophenyl phosphate (26), and several times faster than its *S*-*p*-nitrophenyl isomer (28) : the former observation could be explained by the greater $-E$ effect of oxygen than of sulphur, but it is interesting that in a comparison of the alkaline hydrolysis rates of alkyl acetates and thiolacetates Rylander and Tarbell [17] found that hydrolysis of the thiolacetates requires the greater energies of activation. The second observation cannot be explained in this way. In the *OS*-diethyl compound and its isomer, *p*-nitrothiophenol is a stronger acid than *p*-nitrophenol, and the $(E + I)$ effect of the sulphur atom must be assumed constant. Therefore the *S*-*p*-nitrophenyl compound is expected to be hydrolysed the faster.

These results may be explained by the ready polarizability of sulphur and cyanide. In molecules not containing these groups, the atoms directly bonded to the phosphorus are oxygen, nitrogen, or fluorine, which, by conjugation, increase the negative charge on the phosphorus atom and set up a permanent potential which must be overcome by the approaching hydroxyl ion before a transition complex can be produced. During the formation of the complex, steric changes take place which must affect this potential, but, as the bonds between phosphorus and these atoms may not be readily polarizable, it is likely that the changes in potential are very similar from molecule to molecule. When a

[17] Rylander and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 3021.

polarizable group such as the ethylthio-group is introduced, this is no longer true. The approach of the hydroxyl ion may polarize the P–S bond in the sense $\overset{\delta+}{P}—\overset{\delta-}{S}$, so facilitating the formation of the transition complex. In the *S*-*p*-nitrophenyl compound, however, this leads to some strengthening of the P–S bond, which is therefore hydrolysed more slowly than its *S*-ethyl isomer in spite of the greater strength of the displaced acid. Thus it appears necessary to postulate a time-variable effect in response to the reagent in compounds containing phosphorus–sulphur bonds which is absent or constant in the other compounds considered. Such an effect should be less the less polar the reagent. It is in fact found (following paper) that the rates of hydrolysis in water of diethyl *p*-nitrophenyl phosphate and *OS*-diethyl *p*-nitrophenyl phosphorothiolate and its *S*-*p*-nitrophenyl isomer differ much less than in alkali.

Although there are a few anomalies, the electronic theory, as developed to explain reaction rates in carbon chemistry, apparently applies to a wide range of organophosphorus compounds without major alteration. This is perhaps surprising. Most of the substituents considered are very close to the groups displaced, so that "*ortho*"-effects might be expected; and nothing is known of the configuration of the transition complexes, so that the precise nature of the electromeric effects postulated is doubtful.

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Fisons Pest Control Limited, Chesterford Park Research Station,
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## 739. *The Effects of Substituents on the Rates of Hydrolysis of Some Organophosphorus Compounds. Part II.* Rates in Neutral Solution.*

By D. F. Heath.

The approach used in the preceding paper is extended to cover rates of hydrolysis in compounds under conditions such that catalysis by hydroxyl ions can be neglected. Salts catalyse hydrolysis of *NN'*-di*iso*propyl- and *NN*-dimethyl-*N'*-*iso*propyl-phosphorodiamidic fluoride. $k_w$ for the first compound is probably composite, water acting as both an anionoid and a cationoid reagent.

Generally, however, water acts as an anion by an $S_N2$ mechanism. Substituents have similar effects to those described in Part I, except that in the tetra-alkyl pyrophosphates steric effects are more important than inductive effects, and that P–S–C groups accelerate the rates less in neutral than in alkaline solution.

The purpose of this paper is to discuss the rate constants in neutral solution along similar lines to those used in Part I * for alkaline solution.

The overall hydrolysis constant in neutral solution is made up of five terms:

$$k = k_w + k_{H^+}[H^+] + k_{OH^-}[OH]^- + k_A[A] + k_B[B]$$

where $k_B$ and $k_A$ are the constants for catalysis by general bases and acids respectively. Kilpatrick and Kilpatrick,[1] in their very full study of the hydrolysis of di*iso*propyl phosphorofluoridate, have shown that $k_B$ and $k_A$ are much greater than $k_w$. Heath and Casapieri [2] have shown that phosphate ions catalyse the hydrolysis of *NNN'N'*-tetramethylphosphorodiamidic fluoride. Phosphate buffers also catalyse the hydrolysis of *NN*-dimethyl-*N'*-*iso*propylphosphorodiamidic fluoride. To gain some idea of the magnitude of general catalysis on another compound of this type, the rates of hydrolysis at three temperatures

* Part I, preceding paper.

[1] Kilpatrick and Kilpatrick, *J. Phys. Colloid Chem.*, 1949, **53**, 1371.
[2] Heath and Casapieri, *Trans. Faraday Soc.*, 1951, **47**, 1093.

of *NN'*-di*iso*propylphosphorodiamidic fluoride have been found in two concentrations of phosphate–citrate buffers at pH 5·70. In the study of the di*iso*propyl compound it is found that $k_A + k_B$ (which cannot be separated, as only one buffer system at one pH was used) is much greater than $k_w$, and also that a graph of log $(k_A + k_B)$ against $1/T$ gives a straight line corresponding to an activation energy of 16·0 kcal./mole. When log $k_w$ is plotted against $1/T$, however, the points do not fall on a straight line, and the considerable error in $k_w$, which is the relatively small difference between two numbers, cannot account for the disagreement. This indicates that two reactions occur simultaneously, the balance between them differing with the temperature. The two obvious reactions are :

$$(Pr^iNH)_2PO{\cdot}F + H_2O \longrightarrow (Pr^iNH_2)PO{\cdot}OH + HF$$

$$(Pr^iNH)_2PO{\cdot}F + H_2O \longrightarrow Pr^iNH{\cdot}PO(OH){\cdot}F + Pr^iNH_2$$

The first is analogous to hydrolysis by hydroxyl ion, the second to hydrolysis by hydrogen ions, as studied by Heath and Casapieri.[2]

Three difficulties may thus be encountered in interpreting the published results.

Where rates were determined in water alone, there is the possibility that products may catalyse the hydrolysis. This is characterised in the graph of $-\log A$ against $t$ (where $A$ is the concentration remaining at time $t$) by an increase in slope with increase in $t$. The effect was absent in the results given in the Tables. The present author's results were obtained on very dilute solutions of compounds labelled with $^{32}P$, so that the maximum attainable salt concentration could not influence the rates measurably. Those of Toy [3] on pyrophosphates of the general formula $(RO)_2PO{\cdot}O{\cdot}PO(OR')_2$, where R and R' are alkyl groups, probably do not show the effect because the products are strong acids, so that base-catalysis is ruled out. There is no evidence that the hydrolysis of these pyrophosphates is catalysed by acids.

Where rates were determined in buffer solutions there are generally no data by means of which one can allow for the contribution made by acid–base catalysis. Consequently, while such results are consistent *inter se*, they cannot be compared with results obtained on other compounds in water alone.

Finally, it must be decided whether water is acting as an anionoid or a cationoid reagent, or as both simultaneously. The effect of substituents on acid-catalysed rates is different, and not well understood. In so far as water acts as a cationoid reagent it is analogous in action to hydrogen ions, and the most basic substituent is thus likely to be displaced first. This may however be followed by a rapid breakdown of the rest of the molecule, as in the acid hydrolysis of octamethylpyrophosphoramide.[2] Consequently, unless it is shown that basic groups are not displaced (as Toy [3] did) it cannot be assumed that water is acting solely as an anionoid reagent. Therefore, we must be cautious in interpreting the attack on compounds by water as anionoid when their hydrolyses are catalysed by hydrogen ions. The R–O–P bonding is, however, very stable to acids, so that it is reasonable to suppose that the attack on molecules of the $(RO)_2PO{\cdot}X$ type is anionoid, even when this has not been proved.

## Experimental

*Hydrolysis of* NN'-*Diisopropylphosphorodiamidic Fluoride.*—The rates were followed by the method (*ai*) of the previous paper, with tracer quantities of the compound only. McIlvaine's phosphate–citrate buffer of pH 5·70 was prepared according to the instructions in "Handbook of Chemistry and Physics" (Chemical Rubber Publishing Co., Cleveland), at total molar concentrations of 0·1274 and 0·01274. The pH was checked before and after each run with a Doran pH-meter and a glass electrode against a saturated calomel electrode, and, with one exception, agreed to within 0·01 pH unit of 5·70. The value at the end of the run at 72·9° in the lower concentration was 5·75. By using the set-up as a millivoltmeter the pH at 72·9° was found to be 5·70. The pH is thus independent of temperature.

$k_H$ was found to be 0·656[$H^+$] in 0·005N-hydrochloric acid at 25° [method (*ai*) of Part I]. A similar constant is found for the tetramethyl analogue,[4] for which $E = 14$ kcal./mole. This

[3] Toy, *J. Amer. Chem. Soc.*, 1948, **70**, 3882; 1950, **72**, 2065.

value of $E$ was used to find $k_H$ for the *NN'*-di*iso*propyl compound at different temperatures. ($k_A + k_B$) and $k_w$ are not very sensitive to $E$. $k_{OH}$ was found from the results in Part I.

$k_H$ in Table 1 was calculated by assuming that the secondary salt effect raises the constant 25% at the lower concentration and 100% at the higher. These estimates are based on the

TABLE 1. *Constants for the hydrolysis of* NN'*-di*iso*propylphosphorodiamidic fluoride in phosphate–citrate buffer at* pH 5·70.

| Molarity of buffer | | 25·0° $10^5k$ (min.$^{-1}$) | 50·0° $10^4k$ (min.$^{-1}$) | 72·9° $10^3k$ (min.$^{-1}$) | $E$ (kcal./mole) |
|---|---|---|---|---|---|
| 0·1274 | $k$ | 8·12 ± 0·10 | 6·816 ± 0·048 | 3·687 ± 0·026 | — |
| | $k_H$ | 0·27 | 0·145 | 0·072 | 14 |
| | $k_{OH}$ | 0·02 | 0·010 | 0·006 | 11·2 |
| 0·01274 | $k$ | 1·181 ± 0·015 | 1·040 ± 0·012 | 0·803 ± 0·014 | — |
| | $k_H$ | 0·169 | 0·091 | 0·045 | 14 |
| | $k_{OH}$ | 0·024 | 0·010 | 0·006 | 11·2 |
| 0 (calc.) | | 0·421 | 0·404 | 0·486 | — |
| 1·0 | $k_{A+B}$ | 59·7 | 49·9 | 24·9 | 16·0 ± 0·2 |
| | $k_w$ | 0·228 ± 0·03 | 0·303 ± 0·03 | 0·435 ± 0·03 | — |

activity coefficients of salts given by Robinson and Harned.[4] They must be considerably in error to introduce errors as great as those in the original runs.

$k_{OH}$ is corrected both for the secondary salt effect and the increasing dissociation of water with increase in temperature.

Primary salt effects may lead to systematic errors in $k_{A+B}$, which may affect $E$ for salt-catalysis, and also $k_w$. The influence on the latter is again likely to be unimportant compared with the errors in $k$.

*Hydrolysis Rates in Water* (*see Tables*).—The published and the present results are tabulated; numbering of the compounds continues from Part I.

TABLE 2. *Constants for the hydrolysis in water, at 25°, of some pyrophosphates,* $(RO)_2PO{\cdot}O{\cdot}PO(OR')_2$.

| No. | Compound R | R' | $10^3k$ (min.$^{-1}$) | No. | Compound R | R' | $10^3k$ (min.$^{-1}$) | No. | Compound R | R' | $10^3k$ (min.$^{-1}$) | No. | Compound R | R' | $10^3k$ (min.$^{-1}$) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 37 | Me | Me | 25 | 40 | Et | Et | 1·6 | 43 | Et | Bu$^n$ | 0·95 | 46 | Pr | Pr$^i$ | 0·20 |
| 38 | Me | Et | 7·0 | 41 | Me | Pr$^i$ | 1·1 | 44 | Pr | Pr | 0·65 | 47 | Bu$^n$ | Pr$^i$ | 0·2 |
| 39 | Me | Pr | 5·6 | 42 | Et | Pr | 1·0 | 45 | Et | Pr$^i$ | 0·28 | 48 | Pr$^i$ | Pr$^i$ | >0·09 |

The constant for tetraethyl pyrophosphate is taken from Ketelaar and Bloksma's results.[5] The remainder are taken from the figures given by Toy.[4] Of Toy's results, those for compounds which do not contain di*iso*propylphosphato-groups follow first-order kinetics until hydrolysis is nearly complete. The graph of ln $A$ against $t$ for those which do contain this group is initially a straight line, but curves to a line of lower gradient after 50—90% hydrolysis; this is most readily explained if they contain impurities more stable in water. These rate constants have therefore been calculated from the first straight portion of the curves, with allowance for such impurities. Results obtained in such a way are necessarily of low accuracy. The interpretation of the graph for tetra*iso*propyl pyrophosphate is particularly difficult: 0·09 is the greatest possible value of the constant.

TABLE 3. *Constants for the hydrolysis of some compounds at 37° in* 0·067M*-phosphate buffer at* pH 7·4.

| No. | Compound | $k$ (min.$^{-1}$) | % hydrolysed | No. | Compound | $k$ (min.$^{-1}$) | % hydrolysed |
|---|---|---|---|---|---|---|---|
| 49 | $(EtO)(EtS)PO{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | $8 \times 10^{-4}$ | — | 54 | $(EtO)_2PO{\cdot}O{\cdot}C_6H_4Cl$-*o* | $2·3 \times 10^{-6}$ | 7·9 |
| 50 | $(EtO)_2PO{\cdot}S{\cdot}C_6H_4{\cdot}NO_2$-*p* | $4·7 \times 10^{-4}$ | — | 55 | $(EtO)_2PO{\cdot}O{\cdot}C_6H_4Cl$-*p* | $7·2 \times 10^{-7}$ | 4·2 |
| 51 | $(EtO)_2PO{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*o* | $5·6 \times 10^{-5}$ | 78 | 56 | $(EtO)_2PO{\cdot}OPh$ | $1·6 \times 10^{-7}$ | 2·6 |
| 52 | $(EtO)_2PO{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | $3·9 \times 10^{-5}$ | 65 | 57 | $(EtO)_2PS{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*p* | $7·0 \times 10^{-7}$ | — |
| 53 | $(EtO)_2PO{\cdot}O{\cdot}C_6H_4{\cdot}NO_2$-*m* | $1·4 \times 10^{-5}$ | 45 | | | | |

The results (51)—(56) are given by Aldridge and Davison.[6] It is obvious that some of the results are very inaccurate. The remainder are taken from Aldridge and Davison's work,[7] and are corrected for the contribution made by hydroxyl-ion catalysis. This correction lowers the constant by 32% for compounds (49) and (57), and by 11% for no. (50). The correction to no. (52) would be about 3%.

[4] Robinson and Harned, *Chem. Rev.*, 1941, **28**, 419.
[5] Ketelaar and Bloksma, *Rec. Trav. chim.*, 1948, **67**, 665.
[6] Aldridge and Davison, *Biochem. J.*, 1952, **51**, 62.
[7] *Idem, ibid.*, 1952, **52**, 663.

TABLE 4. *Hydrolysis constants for some fluoro-compounds.*

| No. | Compound | Temp. | $k$ (min.$^{-1}$) | Ref. |
|---|---|---|---|---|
| 60 | $(Pr^iO)_2PO{\cdot}F$ | 25° | $1{\cdot}2 \times 10^{-4}$ | 1 |
| 61 | $(Pr^i{\cdot}NH)_2PO{\cdot}F$ | 25 | $2{\cdot}3 \times 10^{-6}$ | |
| 62 | $(Me_2N)(Pr^i{\cdot}NH)PO{\cdot}F$ | 100 | $1{\cdot}5 \times 10^{-3}$ | |
| 63 | $(O<[CH_2{\cdot}CH_2]_2>N)(EtO)PO{\cdot}F$ | 25 | $4 \times 10^{-7}$ | |

Compounds (61)—(63) were measured in very dilute solution by method (*ai*) of Part I, or are corrected for salt effects. The constants are thus $k_w$ only.

*Triethyl* (58) *and Trimethyl* (59) *Phosphate.*—Cavalier [8] gives $k_w$ for triethyl phosphate as $1{\cdot}15 \times 10^{-4}$ hr.$^{-1}$ at 44°, and $1{\cdot}14 \times 10^{-2}$ hr.$^{-1}$ at 88°, whence at 25° $k = 1{\cdot}7 \times 10^{-7}$ min.$^{-1}$, $E$ = 23·8 kcal./mole. For trimethyl phosphate, Cavalier gives $k = 6{\cdot}32 \times 10^{-2}$ hr.$^{-1}$ = $1{\cdot}05 \times 10^{-3}$ min.$^{-1}$ at 88°.

*Hydrolysis Constants for Some Chloro-compounds.*—Dostrovsky and Halman [9] determined the rates of hydrolysis of five chloro-compounds in aqueous alcohol, and showed that the inductive effects of the substituents are in fair quantitative agreement with the inductive effects of the same substituents in chloroformic esters.

## DISCUSSION

It is convenient to divide the compounds into three groups: the pyrophosphates of Table 2, in which the differences in rate must be due solely to the inductive and steric effects of the different alkyl substituents; those of Table 3, together with triethyl and trimethyl phosphate, where the differences are predominantly due to differences in the acidic groups; and those of Table 4, of compounds containing more complex alterations in the basic substituents.

*Pyrophosphates.*—Both phosphate groups in each molecule are open to attack. Each constant in Table 2 is thus the sum of two constants. If it is assumed that the hydrolysis is an $S_2$ replacement in which the rate is controlled by the rate of attachment of a water molecule to a phosphorus atom, the rates will decrease as the $-I$ effects increase, in the order Me < Et < $Bu^n$ < $Pr^i$. It was shown in Part I, by comparing the pairs (16) and (17), and (14) and (10), that the transmission of effects along the pyrophosphate bonds is slight. Thus the inductive effect of groups on one phosphorus atom has little effect on the reactivity of the other. Therefore, if $k_1$ is the constant for the reaction with one phosphorus, and $k_2$ the constant for the reaction with the other, the total constant ($k$) given in the Table equals $k_1 + k_2$. In some instances $k_1$ and $k_2$ can be found from the rates for the symmetrical compounds. The constant for $(Bu^nO)_2P$ cannot be found in this way, but as *n*-butyl has slightly more $-I$ effect than *n*-propyl, it is reasonable to assume that $k_{Bu} = 0{\cdot}9k_{Pr}$. Comparison of the observed and the calculated constants (Table 5)

TABLE 5. *Observed and calculated constants for some pyrophosphates,* $(RO)_2PO{\cdot}O{\cdot}PO(OR')_2$.

| | Compound | | $10^3k$ (min.$^{-1}$) | | | Compound | | $10^3k$ (min.$^{-1}$) | |
|---|---|---|---|---|---|---|---|---|---|
| No. | R | R′ | obs. | calc. | No. | R | R′ | obs. | calc. |
| 37 | Me | Me | *25* | *25* | 43 | Et | $Bu^s$ | 0·95 | 1·1 |
| 38 | Me | Et | 7·0 | 13·3 | 44 | Pr | Pr | *0·65* | *0·65* |
| 39 | Me | Pr | 5·6 | 12·8 | 45 | Et | $Pr^i$ | 0·28 | 0·85 |
| 40 | Et | Et | *1·6* | *1·6* | 46 | Pr | $Pr^i$ | 0·20 | 0·37 |
| 41 | Me | $Pr^i$ | 1·1 | 12·5 | 47 | $Bu^s$ | $Pr^i$ | 0·20 | 0·34 |
| 42 | Et | Pr | 1·0 | 1·1 | 48 | $Pr^i$ | $Pr^i$ | *0·09* | *0·09* |

Italicized constants were used to determine $k_1$ and $k_2$.

shows satisfactory agreement for compounds (42) and (43) containing neither methyl nor *iso*propyl groups. The discrepancies are most readily explained by steric effects; *n*-alkyl groups other than methyl groups exert a constant steric effect somewhat greater than that of methyl groups, and *iso*propyl groups a very much greater steric effect than any other group, as suggested by Toy.[3] The substitution of two methyl groups for two ethyl groups increased the constant by a factor of only about 3—4 in the compounds discussed in Part I,

[8] Cavalier, *Ann. Chim. Phys.*, 1899, **18**, 449.
[9] Dostrovsky and Halmann, *J.*, 1953, 503.

whereas the equivalent substitution here (absence of P–O–P interaction being assumed) of four methyl for four ethyl groups increases the rate by a factor of 16, a difference most readily explained by steric hindrance by ethyl groups. Steric hindrance by *iso*propyl groups is the simplest explanation of the slow hydrolysis of di*iso*propyl fluorophosphate (2), discussed in Part I. Of course, the assumption of no P–O–P interaction is not justifiable. Doubtless such interaction contributes to the results, but if this alone is to explain them then the unlikely assumption must be made that groups on one phosphorus atom exert as great an inductive effect on the other phosphorus atom as on that to which they are attached.

Why methyl and ethyl groups should exert different steric effects in these molecules and not in those studied in Part I is not clear. Perhaps the P–O–P system is considerably more rigid, owing to its partially double-bonded character, than most of the P–X bonds previously considered. This may make it more difficult for the molecule to accommodate itself in the transition state. Whatever the reason, it appears that steric effects are more important than inductive effects in this series of compounds, but that inductive effects also operate.

*Compounds of Table* 3.—The constants are comparable *inter se*, but, being determined in buffer solutions, cannot be compared with those in the other Tables. The effects of substituents in the aromatic ring are as would be expected from the structure of the molecules. The hydrolysis is a side-chain reaction with respect to the benzene ring, so that electromeric effects will be less important than inductive effects. Thus a nitro-group will exert a greater $+I$ effect than a chlorine atom, and a chlorine atom a greater one than a hydrogen atom. As however the P–O–C ester system is to some extent conjugated, as can be deduced from the electromeric effects described in Part I, electromeric effects will somewhat modify the inductive effects, causing *o*-nitro- and *p*-nitro- to be more positive than *m*-nitro-groups. *ortho*-Groups produce greater effects than *para*-groups in the absence of steric hindrance or specific interaction between neighbouring groups. These considerations lead to the observed order, in which the rates increase as the $-(I + E)$ effects decreases, *viz.*, H, *p*-Cl, *o*-Cl, *m*-$NO_2$, *p*-$NO_2$, *o*-$NO_2$.

It is interesting that diethyl phenyl phosphate (56) is hydrolysed at a very similar rate to triethyl phosphate (58), although the phenyl group usually exhibits a weak $+I$ effect.

The substitution of P=S for P=O inhibits hydrolysis by water [cf. nos. (57) and (52)] rather more than by hydroxyl ions [nos. (20) and (26)], but qualitatively the effect is the same.

It is notable that, while the order of the constants for *OS*-diethyl *O*-*p*-nitrophenyl phosphorothiolate (49), *OO*-diethyl *S*-*p*-nitrophenyl phosphorothiolate (50), and diethyl *p*-nitrophenyl phosphate (52) is the same for hydrolysis by both water and hydroxyl ions, the differences are much less in water. That the ethylthio-group should be more activating than the phenylthio-group still appears to require some such explanation as that proposed in Part I. In accordance with that hypothesis the constants for all three compounds are closer for reactions with the less polar reagent.

*Compounds of Table* 4.—There are too few in this group for general conclusions to be drawn. Kilpatrick and Kilpatrick [1] assumed that in the hydrolysis of di*iso*propyl phosphorofluoridate (60) water acted as an acid, not as a base. There are reasons for believing this may be true in the hydrolysis of *NN'*-di*iso*propylphosphorodiamidic fluoride (61). It is interesting that the first compound is hydrolysed in water about 50 times as rapidly as the second, whereas in alkaline solution the rates are about equal [nos. (2) and (3)]. It is also certain that at the same temperature *NN*-dimethyl-*N'*-*iso*propyl-phosphorodiamidic fluoride (62) would be hydrolysed more rapidly than ethyl morpholino-phosphorofluoridate (63), although a dimethylamino-group exerts a greater $-I$ effect than a morpholino-group (see Part I) and *iso*propylamino- a greater $-I$ effect than an ethoxy-group. Such differences may indicate that these compounds are not hydrolysed by the same mechanism in water and in alkaline solution.

*General Conclusions.*—While a combination of steric, inductive, and electromeric effects accounts for the observed rates of hydrolysis in water of most of the compounds studied, and the effects in these instances are consistent with water's acting as an anionoid reagent

which replaces the most acidic radical by an $S_2$ mechanism, there are instances, possibly confined to phosphoroamidic compounds, in which water probably acts as a cationoid reagent, and the general rules then do not hold.

FISONS PEST CONTROL LIMITED, CHESTERFORD PARK RESEARCH STATION, LITTLE CHESTERFORD, NR. SAFFRON WALDEN, ESSEX. [*Received, March 16th*, 1956.]

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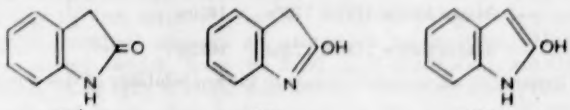
## 740. *Vibrational Frequency Correlations in Heterocyclic Molecules. Part II.*[1] *Infrared Spectra and Structure of Oxindole and Related Compounds.*

By A. E. KELLIE, D. G. O'SULLIVAN, and P. W. SADLER.

Infrared spectra of oxindole, phthalimidine, phthalimide, and related molecules in chloroform strongly support fully ketonic formulæ for all these compounds. Intermolecular hydrogen bonding is also present provided the NH group remains unsubstituted. The carbonyl stretching frequencies of oxindole vary with the substituents in the benzene ring, probably being dependent on their σ-values. The effect of these substituents is transmitted through the NH group to the carbonyl group. Other features of the spectra of these compounds are discussed in relation to the spectra of substituted isatins.

STRUCTURES containing NH and CO groups in five-membered rings are often present in naturally occurring compounds and vibrational spectra have frequently been used in their investigation. However, reference data are still sketchy and to supplement previous work on substituted isatins,[1] and provide further basic information, infrared spectra of some oxindoles and related compounds have been obtained. Vibrational spectra have been used in investigating the spiro-structures that arise in degradation products of certain alkaloids which are structurally related to oxindole.[2]




(I) (II) (III)

There are three possible formulæ for oxindole. Chemical evidence was assumed by Julian, Pikl, and Wantz [3] to favour the predominance of the lactam form (I), but (II) and (III) were also considered to be present in solution. Bergmann [4] thought that the infrared spectrum of oxindole in Nujol mull supported this view. However, the sole spectral evidence for the existence of an enolic structure, the presence of absorption at 1165—1135 cm.$^{-1}$, can be given alternative interpretations. Ultraviolet spectra of oxindole and its 1-methyl and 1 : 3 : 3-trimethyl derivatives are very similar,[5] suggesting that all these compounds exist in a ketonic form. However, early controversy on the ultraviolet spectrum of isatin [6] shows that this evidence is equivocal. From their chemical behaviour, phthalimidine and phthalimide have always been assigned fully ketonic structures although lactam–lactim tautomerism is possible in both cases.

[1] The paper by O'Sullivan and Sadler, *J.*, 1956, 2202, is regarded as Part I.
[2] Loudon, "Recent Work on Naturally Occurring Nitrogen Heterocyclic Compounds," *Chem. Soc. Special Publ.*, 1955, No. 3, p. 12; Stevens, *ibid.*, p. 19; Markees and Burger, *J. Amer. Chem. Soc.*, 1949, **71**, 2031; Kates and Marion, *ibid.*, 1950, **72**, 2308.
[3] Julian, Pikl, and Wantz, *ibid.*, 1935, **57**, 2026.
[4] Bergmann, *ibid.*, 1955, **77**, 1549.
[5] Ramart-Lucas and Biquard, *Bull. Soc. chim. France*, 1935, **2**, 1383.
[6] Morton and Rogers, *J.*, 1925, 2698; Dabrowski and Marchlewski, *Bull. Soc. chim. France*, 1933, **53**, 946; Ault, Hurst, and Morton, *J.*, 1935, 1653.

## Results and discussion

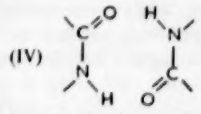
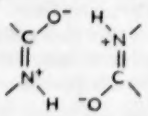
Table 1 shows that all except the *N*-methyl compounds possess a fairly sharp peak at 3478—3444 cm.$^{-1}$ and a broad maximum at 3320—3220 cm.$^{-1}$, and every compound shows intense absorption in the 1772—1680 cm.$^{-1}$ region. Maxima near 3450 cm.$^{-1}$ are usually attributed to stretching vibrations of the NH group and a broad band at 3250 cm.$^{-1}$ to NH groups involved in hydrogen bonding.[7] Absorption at 1772—1680 cm.$^{-1}$, which is at too high a frequency to be associated with C=N or C=C vibrations under normal conditions, must be assigned to the CO stretching mode. This is discussed in more detail below. Only weak absorption occurs with the *N*-methyl compounds at 3500—3400 cm.$^{-1}$ which may be the first carbonyl harmonic.[8] The three bands are present in 3 : 3-dichloroxindole in which keto–enol tautomerism is presumably absent, and the 1700 cm.$^{-1}$ band is

Table 1. *Infrared maxima in chloroform.*

| | 4000—3000 cm.$^{-1}$ | | | 1800—1650 cm.$^{-1}$ | | 1650—1290 cm.$^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Oxindole | — | 3462m | 3220w | 1725s | 1708s | 1627m | — | 1472m | — | 1356w | 1329w |
| 1-Methyloxindole | — | — | — | 1700s | | 1619m | — | 1468w | 1373w | 1354m | 1310w |
| 3 : 3-Dichloro-oxindole | — | 3448m | 3250w | 1758s | | 1624m | — | — | — | 1324w | — |
| 3 : 3-Dichloro-1-methyloxindole | — | — | — | 1739s | | 1616m | — | 1472w | 1370w | 1351w | — |
| *p*-Chloroacetamidophenol | 3625w | 3420m | 3320w | 1680s | | 1609w | 1520w | 1480w | — | 1328w | — |
| 5-Hydroxy-oxindole * | — | — | — | 1700m | | — | — | — | — | — | — |
| 5-Methyloxindole | — | 3460m | 3230w | 1718s | 1700s | 1621w | 1612w | — | 1460w | — | 1313w |
| 5-Chloro-oxindole | — | 3450m | 3220w | 1731m | | 1623m | — | 1460w | — | — | — |
| 5-Bromo-oxindole | — | 3450m | 3220w | 1733m | | 1620w | — | 1465w | — | 1340w | 1292w |
| 5-Nitro-oxindole | — | 3445m | 3270w | 1754s | 1722s | 1630w | 1608w | — | 1475w | — | 1343s 1290w |
| Phthalimidine | — | 3478m | 3240w | 1698s | | 1621w | — | 1458w | — | 1333w | 1304w |
| Phthalimide | — | 3444m | 3230w | 1775m | 1735s | 1608w | — | — | — | 1379m | 1308m |
| *N*-Methylphthalimide | — | — | — | 1772m | 1712s | 1620w | 1605w | — | 1430w | 1387s | — — |
| 3-Nitrophthalimide | — | 3440m | 3230w | 1778m | 1737s | 1620w | — | — | — | 1350s | — |
| 4-Nitrophthalimide | — | 3445m | 3230w | 1780m | 1736s | 1622w | — | — | — | 1350s | — |

* NH frequencies not recorded because of the low solubility of this compound.

still present in 3 : 3-dichloro-1-methyloxindole which can only exist in the ketonic form. Of the compounds listed, only *p*-chloroacetamidophenol exhibits an unassociated OH absorption at 3625 cm.$^{-1}$, the solubility of 5-hydroxyoxindole being too low to permit the recording of an OH frequency for this compound. It must be concluded, therefore, that all these substances exist in the fully ketonic form. The hydrogen bonding which occurs when an NH group is present is most likely to be intermolecular bonding, similar to that present in isatin,[1] with (IV) and (V), representing relevant parts of two adjacent molecules, contributing to the structure of the, probably dimeric, hybrid.

(IV)   (V)

Absorption at about 1620 cm.$^{-1}$, present in every case, is produced by CC stretching vibrations of the benzene ring.[9] In isatins [1] this absorption is of similar intensity to that

[7] (*a*) Richards and Thompson, *J.*, 1947, 1248; (*b*) Witkop, *J. Amer. Chem. Soc.*, 1950, **72**, 614; Witkop and Patrick, *ibid.*, 1951, **73**, 1558; Darmon and Sutherland, *Nature*, 1949, **164**, 440.
[8] Jones, Williams, Whalen, and Dobriner, *J. Amer. Chem. Soc.*, 1948, **70**, 2031.
[9] Colthup, *J. Opt. Soc. Amer.*, 1950, **40**, 397.

of the carbonyl groups. Here, however, the strongest absorption is shown by oxindoles unsubstituted in the benzene ring, but even these possess only half the carbonyl intensities. Splitting of the 1620 cm.$^{-1}$ frequency occurs in isatins which possess *meta*- or weakly *para*-directing substituents in the benzene ring and this feature is also present in oxindoles (Table 1) and acetanilides (Table 3).

Bands in the 1480—1430 cm.$^{-1}$ region have the frequency range associated with $CH_2$ or $CH_3$ deformation modes [10] and as they are absent in 3 : 3-dichloro-oxindole, phthalimide, and 3- and 4-nitrophthalimide they may reasonably be attributed to these groups. The existence of this absorption in oxindoles and phthalimidine further supports the ketonic structure for these compounds.

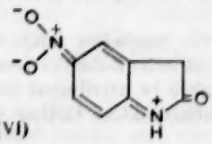
It was previously considered [1] that bands in the 1350 cm.$^{-1}$ region might be associated with the Ph–N linkage, but it now becomes apparent that various sources are responsible. The fairly intense peak at 1350—1340 cm.$^{-1}$ in the nitro-compounds owes its presence to the nitro-group.[11] A corresponding band at 1340 cm.$^{-1}$ exists for 7-nitroisatin. Maxima which appear for the *N*-methyl compounds at 1387—1370 cm.$^{-1}$ and the maximum at 1372 cm.$^{-1}$ for *N*-methylisatin are probably N–Me deformation frequencies.[12] Other peaks in the 1350—1300 cm.$^{-1}$ region probably owe their origin to Ph–N or Ph–C vibrations.

The carbonyl maxima of these compounds show features of considerable interest. The phthalimides all show two very sharp and intense peaks, the lower- being about twice the intensity of the higher-frequency absorption. The possibility that one maximum is due to free and the other to hydrogen-bonded carbonyl groups is virtually eliminated as the character of the peaks is unchanged in the *N*-methyl compound. A similar phenomenon occurs with symmetrical acid anhydrides,[13] the two carbonyl peaks sharing an almost constant separation of 60 cm.$^{-1}$, and with symmetrical diacyl peroxides [14] in which these peaks are separated by about 20 cm.$^{-1}$. This feature undoubtedly arises from coupling between identical characteristic vibrations of the two carbonyl groups. The frequency separation with benzoyl peroxides is substantially independent of the nature of substituents. The results in Table 1 suggest that substituents in the benzene ring have little effect on the carbonyl frequencies of phthalimide. Oxindole and some substituted oxindoles, possessing a single carbonyl group, show two peaks in the carbonyl region. Here the higher-frequency maximum is very sharp and intense whilst the lower-frequency absorption is slightly less intense. As the *N*-methyl compounds possess a single peak, partial hydrogen bonding appears an attractive explanation. However, 5-halogeno-substituted compounds, which, from the 3220 cm.$^{-1}$ absorption, are the most extensively hydrogen bonded, show only a single maximum. Differing absorption frequency for free and bonded carbonyl groups does not account for the presence of only a single peak in other cases, *e.g.*, for phthalimidine. It should be noted that aceto-*o*-toluidide, which shows structural similarities to oxindole, also possesses two carbonyl absorptions both in dioxan and in the solid state, the two absorptions being more pronounced in the solid.[7a] Postulating vibrational coupling between the carbonyl groups in the dimer also does not account for all the above features. The possibility that another linkage produces, independently of the carbonyl group, one of these peaks is also unlikely.[15]

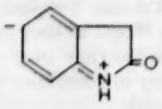
Although the number of oxindoles considered is too small for unassailable conclusions to be reached here, certain points deserve comment. A strongly *ortho-para*-directing group in the 5-position gives rise to a unique maximum and the separation of the maxima in other cases increases with the tendency of the substituent to withdraw electrons from the ring. Groups that favour the formation of structures such as (VI) and (VII) produce two maxima. Thus the appearance of a second peak may well be related to the effective

[10] Thompson and Torkington, *Proc. Roy. Soc.*, 1945, *A*, **184**, 3; *Trans. Faraday Soc.*, 1945, **41**, 246.
[11] (*a*) Barnes, Gore, Liddel, and Williams, "Infra-red Spectroscopy," Reinhold Publ. Corpn., New York, 1944; (*b*) Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 70.
[12] Ref. 11*b*, p. 221.
[13] Randall, Fowler, Fuson, and Dangl, "Infra-red Determination of Organic Structures," Van Nostrand, New York, 1949.
[14] Davison, *J.*, 1951, 2456.
[15] Yates, Ardao, and Fieser, *J. Amer. Chem. Soc.*, 1956, **78**, 650.

conjugation and to the acquirement of positive charge by the nitrogen atom of the NH group. The latter performs some essential function as this splitting does not occur in phthalimidine or in aromatic ketones.[1,16] Its presence in oxindoles also considerably



(VI)



(VII)

enhances the effect of substituents on the magnitude of the carbonyl frequencies. Two carbonyl peaks are present in benzoyl chloride and have been considered by Rasmussen and Brattain [17] to be caused by either partial association or interaction with a low thermally excited vibration. It seems possible, however, that an increase in quinonoid character of the ring may have some influence in this case also.

In Table 2, carbonyl frequencies of oxindoles are compared with Hammett's σ-values [18] for the substituents in relation to their position with respect to the NH group. The higher-frequency maxima very accurately obey the equation $\nu - \nu_0 = 37{\cdot}5\sigma$, where $\nu_0 = 1725$. Unfortunately oxindoles substituted in other positions were not available to verify fully this linear dependence.

In a previous discussion of the two carbonyl peaks of substituted isatins,[1] it was shown that the lower-frequency maxima could be correlated with the σ-values of the substituents with reference to the β-carbonyl group. The assignment of these frequencies is further confirmed, and the above argument for oxindole strengthened, by the observation that the higher-frequency maxima of isatins are approximately linearly related to the σ-values

TABLE 2. *Hammett's σ values, with reference to the* NH *group, and* α-CO *frequencies of isatins and oxindoles.*

| *a*, Substituent | | | | | | 5-MeO | 5-Me | 4-Me | 6-Me | None | 5-F |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *b*, σ | | | | | | −0·268 | −0·170 | −0·069 | −0·069 | 0 | 0·062 |
| *c*, α-CO frequency (isatins) | | | | | | 1757 | 1758 | 1758 | 1755 | 1755 | 1755 |
| *d*, " Free " CO frequency (oxindoles) | | | | | | — | 1718 | — | — | 1725 | — |
| *e*, " Conjugated " frequency (oxindoles) | | | | | | — | 1700 | — | — | 1708 | — |
| *a* | 6-MeO | 5-Cl | 5-Br | 6-F | 4-I | 6-I | 4-Cl | 6-Cl | 4-Br | 6-Br | 5-$NO_2$ |
| *b* | 0·115 | 0·227 | 0·232 | 0·337 | 0·352 | 0·352 | 0·373 | 0·373 | 0·391 | 0·391 | 0·778 |
| *c* | 1756 | — | — | 1764 | 1762 | 1765 | 1765 | 1765 | 1765 | 1765 | — |
| *d* | — | 1731 | 1733 | — | — | — | — | — | — | — | 1754 |
| *e* | — | — | — | — | — | — | — | — | — | — | 1722 |

of substituents with reference to the NH group. Slight departures from the straight line exist for low σ-values. The α-carbonyl frequency of 6-chloroisatin was previously quoted [1] as 1755 cm.$^{-1}$, where a shoulder is present. However, a second shoulder also occurs at 1765 cm.$^{-1}$ and it now appears likely that the latter is the α-carbonyl frequency and the former is possibly a hydrogen-bonded carbonyl frequency. Very indistinct shoulders are present on some other bands in both the isatin and the oxindole series and may arise from this cause. The influence of substituents on the higher " free " CO frequency is much more marked with oxindoles than with isatins. The lower frequency, which we suggest arises in some way owing to conjugation involving the carbonyl group, does not appear to be linearly related to the σ-constants.

Certain supplementary data are collected in Table 3. The insertion of a nitro-group in the ring has little effect on the carbonyl maximum of phenylacetamide, confirming that the transmission of the effect of substituents occurs through the NH group in oxindoles. From Table 3 it is also seen that the shifts in carbonyl frequency produced by substituents in acetanilide are much smaller than the corresponding shifts in oxindoles. Also,

[16] Fuson, Josien, and Shelton, *J. Amer. Chem. Soc.*, 1954, **76**, 2532.
[17] Rasmussen and Brattain, *ibid.*, 1949, **71**, 1078.
[18] Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 188.

acetanilides in chloroform give sharp bands and show no evidence of splitting. The difference is probably related to the presence of free rotation at the Ph–N and HN–CO bonds in acetanilide and its absence from the planar oxindole molecule. Much bigger substitution shifts occur with solid acetanilides,[7a] where this rotation is either restricted or absent. Oxindole's 5-membered ring may influence the magnitude of the frequency shifts. A study of analogous 6-membered ring compounds is in progress.

TABLE 3. *Maxima in the* 1800—1550 *cm.*$^{-1}$ *region for amides in chloroform.*

| | | | | | | |
|---|---|---|---|---|---|---|
| Phenylacetamide ..... | 1678 | 1589 | *p*-Chloroacetanilide ..... | 1688 | 1598 | |
| *p*-Nitrophenylacetamide ..... | 1682 | 1600 | *m*-Nitroacetanilide ..... | 1696 | 1618 | 1598 |
| Acetanilide ..... | 1685 | 1601 | *p*-Nitroacetanilide ..... | 1698 | 1605 | 1595 |

Correlations of frequencies with σ-values may perhaps be useful for the assignment of certain frequencies in other aromatic compounds.

Comparison of the spectra of isatin, oxindole, 3 : 3-dichloro-oxindole, and phthalimide with the spectra of the *N*-methyl compounds shows that the presence of the methyl group lowers the frequency of the adjacent carbonyl group by about 20 cm.$^{-1}$ in agreement with the behaviour of other amides.[7a] The lower-frequency carbonyl absorption of oxindole is eliminated when this methyl group is introduced. Introducing chlorine substituents into the 3-position produces the usual frequency increment.[19]

## EXPERIMENTAL

Spectra were determined by means of a Perkin-Elmer 21 double-beam recording spectrometer fitted with a rock-salt prism. Results for the 4000—3000 cm.$^{-1}$ region were determined, where possible, for $10^{-2}$M-solutions. For the lower frequencies, $10^{-2}$M-solutions were subjected to three-fold dilution.

Oxindole and 5-methyloxindole were prepared by the Stollé synthesis from ω-chloroacetanilide and ω-chloroaceto-*p*-toluidide respectively.[20] An attempt to make 5-methoxyoxindole by this method at the standard temperature (225°) gave *p*-chloroacetamidophenol, but this was converted [21] into 5-hydroxyoxindole in poor yield by aluminium chloride at 240°. *p*-Chloro-ω-chloroacetanilide was unchanged by aluminium chloride at 225°, but at 250° gave 5-chloro-oxindole [22] in poor yield. 5-Nitro- and 5-bromo-oxindole were prepared by direct nitration [23] and bromination [24] respectively. Treatment of isatin and *N*-methylisatin with phosphorus pentachloride gave 3 : 3-dichloro- and 3 : 3-dichloro-1-methyl-oxindole respectively.[25]

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[19] Hartwell, Richards, and Thompson, *J.*, 1948, 1436; Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; Djerassi and Scholz, *ibid.*, 1948, **70**, 1911; Jones, Humphries, and Dobriner, *ibid.*, 1950, **72**, 956; Jones, Ramsey, Keir, and Dobriner, *ibid.*, 1952, **74**, 80; Jones, Ramsey, Herling, and Dobriner, *ibid.*, p. 2828.
[20] Stollé, *J. prakt. Chem.*, 1930, **128**, 1; Giovannini and Portmann, *Helv. Chim. Acta*, 1948, **31**, 1381.
[21] Beer, Davenport, and Robertson, *J.*, 1953, 1263.
[22] Wahl and Féricéan, *Compt. rend.*, 1928, **186**, 379.
[23] Sumpter, Miller, and Magan, *J. Amer. Chem. Soc.*, 1945, **67**, 499.
[24] Sumpter, Miller, and Hendricks, *ibid.*, p. 1656.
[25] Hantzsch, *Ber.*, 1921, **54**, 1254.

## 741. *Studies in Peroxidase Action. Part XI.* The Oxidation of a Mixture of Amines.*

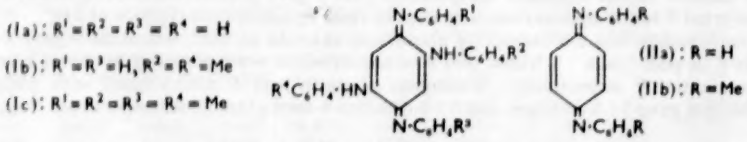
By G. M. K. Hughes and B. C. Saunders.

The products obtained by the oxidation of aniline and of *p*-toluidine separately are well established. The peroxidase oxidation of the two together has now been investigated, and it has been shown that (apart from 4 : 4′-dimethylazobenzene) none of the products from each amine separately has been obtained, but instead compounds of " intermediate " structure.

Previous papers in this series have dealt with the oxidation of single substrates by hydrogen peroxide in the presence of peroxidase. For example, peroxidase oxidation of aniline alone [1] gives rise to 2-amino-5-anilino-*p*-benzoquinone dianil, *pseudo*mauveine, induline, and an " ungreenable " aniline black; that of *p*-toluidine alone [2] gives 4-amino-2 : 5-toluquinone di-*p*-tolylimine, 4-*p*-toluidino-2 : 5-toluquinone bis-*p*-tolylimine, 4 : 4′-dimethyldiphenylamine, and small quantities of 4 : 4′-dimethylazobenzene and 2 : 5-toluquinone *p*-tolylimine. It is therefore of interest to oxidise the two amines together to determine whether or not the separate products of the single oxidations are formed. Such results might provide further evidence concerning the mechanism of the reaction.[3]

The experimental procedure followed closely that established for the oxidation of single amines as substrates. It soon became apparent, however, that the " mixed " oxidation, if allowed to proceed too far, gave tarry products of high molecular weight : since these arose from simpler intermediates, subsequent oxidations were allowed to proceed to only 20% completion; at this stage a clean solid had separated.

The product was split into fractions by solvent extraction, and each fraction examined chromatographically. A large number of compounds was formed, many, however, only in traces. We were able to isolate in significant amounts : 4 : 4′-dimethylazobenzene and substances (A), (B), and (C).




Substance (A) was isolated as red needles, m. p. 237°, though some specimens had m. p.s over the range 223° to 243°. It was obvious, therefore, that a careful investigation was required. Elementary analysis, *C*-methyl analysis, and molecular weight determinations gave a formula $C_{30}H_{28}N_4Me_2$. Physical properties and general chemical behaviour suggested that substance (A) was a dimethyl derivative of azophenine (Ia).

To assist in locating the methyl groups, azophenine (Ia), the di-*p*-methylazophenine (Ib) and tetra-*p*-methylazophenine (Ic) were prepared. *NN*′-Diphenyl-*p*-phenylenediamine was oxidised by mercuric oxide to quinone dianil (IIa) which with *p*-toluidine gave the azophenine (Ib). The same compound was prepared independently by treating quinone di-*p*-tolylimine (IIb) with aniline. However, it was found that if the reaction time for these additions was longer than five minutes, the two products were not identical, having different infrared spectra and giving a depressed mixed m. p. To investigate this further, the di-imine (IIb) was treated with *p*-toluidine for (*a*) five minutes and (*b*) one hour. The products were identical, namely, tetra-*p*-methylazophenine (Ic). Pure azophenine (Ia) was then prepared from the di-imine (IIa) and aniline. With the spectra of these compounds it was possible to interpret with precision the course of the earlier reactions.

* Part X, *J.*, 1956, 940.

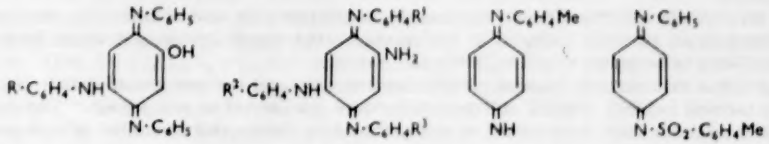
[1] P. J. G. Mann and Saunders, *Proc. Roy. Soc.*, 1935, *B*, **119**, 47.
[2] Saunders and P. J. G. Mann, *J.*, 1940, 769.
[3] Hughes and Saunders, *J.*, 1954, 4630.

It was clear that the addition of *p*-toluidine to the di-imine (IIa) gave initially the required di-*p*-methylazophenine (Ib), but subsequently replacement of the imine groups occurred so that the product was progressively converted into tri- and tetra-*p*-methylazophenine. Similarly the reaction of aniline with the tolylimine (IIb) leads, ultimately, to azophenine (Ia).

Comparison of the infrared spectra of the product (A) from peroxidase action with those of the products obtained as just described showed that it was a mixture of *p*-methylated azophenines.

The light absorption of azophenine (I) is of interest in that the longest-wavelength maxima (*ca.* 390 mμ) are at shorter wavelengths than those in the corresponding anils (II), indicating the chromophore Ar·N:C·CH:CH·C:N·Ar present in the imine is suppressed in the azophenine. This suggests that there is considerable steric strain between adjacent aromatic rings, and this was borne out when models showed that the molecules are far from planar.

Compound (B) was isolated as red needles, m. p. 215—217°. Elementary analysis and molecular weight determination gave $C_{25}H_{21}ON_3$, and its colour reactions with concentrated sulphuric acid suggested strongly that it was a homologue of 2-hydroxy-5-anilino-*p*-benzoquinone dianil [4] (III; R = H).




(III) (IV) (V) (VI)

Heller [5] described the compound (III; R = Me), m. p. 214°, and repetition of his work yielded a product identical with that obtained by peroxidase action. (We have changed the earlier name of 2 : 5-dianilino-*p*-benzoquinone mono-*p*-tolylimine to 2-hydroxy-5-*p*-toluidino-*p*-benzoquinone dianil, for the infrared spectra of this and allied compounds exhibit no maxima corresponding to a carbonyl group. The spectra of allied compounds known to contain this type of carbonyl group all show maxima between 6·07 and 6·10 μ.)

Compound (C) was isolated as red needles, m. p. 173—174°, and had a partial formula $C_{24}H_{19}N_4$·Me. Its colour reactions with concentrated sulphuric acid suggested a mono-*p*-methyl analogue of 2-amino-5-anilino-*p*-benzoquinone dianil [6] (IV; $R^1 = R^2 = R^3 = H$) (again we have changed the name, for compounds of this type exhibit three maxima in the 3 μ region).

None of the three chemical methods that suggested themselves to us for determining which of the three R groups was methyl yielded satisfactory results. We were unable to hydrolyse the compound (C) to simple products. Since it has already been shown that the substance (IV; $R^1 = R^2 = R^3 = OMe$) is not readily hydrolysed in a simple manner [7] it is possible that the early work of Goldschmidt and Wurzschmitt [8] is in error.

Compounds of this type react with amines to give azophenines. Although compound (C) reacted with both aniline and *p*-toluidine, the products were mixtures, and the infrared spectrum of the product from *p*-toluidine action showed that it was a mixture of poly-*p*-methylated azophenines. It appeared therefore that the other groups suffered replacement as readily as did the amino-group.

Lastly, it was not possible to synthesise either the compound (C) or one of its derivatives. Although *p*-benzoquinone imine *p*-tolylimine (V) was prepared successfully, it did not react

[4] Zincke and Von Hagen, *Ber.*, 1885, **18**, 787.
[5] Heller, *Annalen*, 1919, **418**, 265.
[6] Bornstein, *Ber.*, 1901, **34**, 1268.
[7] Daniels and Saunders, *J.*, 1951, 2112.
[8] Goldschmidt and Wurzschmitt, *Ber.*, 1922, **55**, 3216.

with aniline in a simple manner. Again, working with the model compound toluene-*p*-sulphonimido-*p*-benzoquinone anil (VI), it was not possible to add aniline before replacement of the toluene-*p*-sulphonimido- by an anilino-group. This result is in agreement with the findings of Adams and Schowalter.[9]

Although compound (C) has not yet been synthesised, the above work has given a sufficiently large number of reference compounds to interpret in detail its infrared spectrum. This shows that the compound has a *p*-toluidino-group *para* to an amino-group and so is 2-amino-5-*p*-toluidino-*p*-benzoquinone dianil (IV; $R^1 = R^3 = H$, $R^2 = Me$).

## Experimental

Infrared spectra were determined on a Perkin–Elmer Model 21 spectrophotometer, as mulls in Nujol. Light absorption spectra were determined on a Unicam Model S.P. 600 spectrophotometer.

*Peroxidase-catalysed Oxidation of Equimolar Quantities of Aniline and* p-*Toluidine.*—Aniline (4·65 g., 0·05 mole) and *p*-toluidine (5·35 g., 0·05 mole) were dissolved in acetic acid (12 ml.) and diluted with water (500 ml.). The pH was adjusted to 4·5 and hydrogen peroxide (2 ml.; 20-vol.) added. There was no visible change. The addition of enzyme (2 ml.; P.N. *ca.* 3—5), however, produced an immediate dark red colour, and after about 5 min. a pale brown precipitate was formed.

At hourly intervals the effects of enzyme, hydrogen peroxide, and of both reagents together, were determined on small samples of the mixture; the result determined which reagent or reagents were to be added to the bulk reaction mixture.

The initial fast reaction became progressively slower, and the precipitate darker, and ultimately tar was formed. Hence, the oxidations were not carried to completion. The material used in the examination detailed below was obtained by conducting a number of oxidations to one-fifth completion.

Filtering the reaction mixture through " Hyflo Supercel " gave a clear, deep permanganate-coloured solution. This was distilled, and from the distillate unchanged amines were recovered. During the distillation a mauve-black precipitate was formed which was examined chromatographically. It was a complex mixture containing traces of a large number of unidentified compounds of the induline type.

The red filtrate (above) was extracted with chloroform, and the extract, on evaporation, gave a red gum (31 mg. from 50 g. of mixed amines). This was chromatographed on alumina, giving a green solid (22 mg.), which dissolved in ethanol to give a red solution. Qualitatively the light absorptions of this compound and phenosafranine in ethanol, and in dilute hydrochloric acid solution, were similar, but not identical.

*Examination of the solid oxidation product.* The solid (27·7 g.), together with " Hyflo Supercel " (24·8 g.), was extracted (Soxhlet) with light petroleum (b. p. 40—60°; 7 × 750 ml. + 7 × 300 ml.). The combined red extracts were concentrated under reduced pressure, benzene (150 ml.) was added, and the evaporation continued. The tarry residue was freed from solvents at 80°/2 mm. during 8 hr. The black residue (19·7 g., 71%) was dissolved in benzene (350 ml.) and light petroleum (b. p. 40—60°; 200 ml.), and the solution examined as described below (fraction i).

The black petroleum-insoluble material was extracted (Soxhlet) with ether (750 ml.), and the extract on evaporation gave another black residue (5·68 g., 20%) (fraction ii).

The remaining 9% of the original product proved intractable.

Fraction (i). A portion (150 ml.) of the benzene–petroleum solution was chromatographed on alumina (7 × 35 cm.), the column being eluted successively with light petroleum (b. p. 40—60°)–benzene (50, 60, 70% benzene) mixtures, benzene, and benzene–ethanol (1, 2, 5% ethanol) mixtures.

The lowest bands on the column were yellow, green, and pale brown respectively. These were succeeded by a number of dark bands, one of which was separated from the remainder by further chromatography with benzene as eluant. Evaporation of the four eluates gave, in order, 4 : 4′-dimethylazobenzene and substances (A), (B), and (C).

4 : 4′-Dimethylazobenzene was obtained as yellow-orange crystals, m. p. 135° (180 mg.). After two recrystallisations from light petroleum (b. p. 40—60°) and sublimation the m. p. was 137—141° (Found : C, 79·8; H, 6·5; N, 13·5. Calc. for $C_{14}H_{14}N_2$ : C, 80·0; H, 6·7; N, 13·3%).

[9] Adams and Schowalter, *J. Amer. Chem. Soc.*, 1952, **74**, 2597.

In concentrated sulphuric acid, it gave a deep orange solution. An authentic sample was prepared by the following improvement of Barsilowsky's [10] method.

A solution of potassium ferricyanide (164·5 g.) and potassium hydroxide (42·0 g.) in water (1·8 l.) was added to a stirred solution of *p*-toluidine hydrochloride (37·0 g.) in water (500 ml.) during 1 hr. The tarry red precipitate was filtered off, washed, and dried (20·0 g.). Extraction (Soxhlet) with light petroleum (b. p. 40—60°; 750 ml.), and evaporation of solvent gave a black crystalline residue (12·8 g.), which was chromatographed in benzene (215 ml.) on alumina, with light petroleum (b. p. 40—60°)–benzene (1 : 1) as eluant. The first band gave, on evaporation, yellow-orange crystals of 4 : 4′-dimethylazobenzene, m. p. 138—141°, which on recrystallisation from light petroleum had m. p. 141—143°, mixed m. p. with enzyme product 139—142.°

*Identification of Substance* (A).—The red crystalline residue (288 mg.) containing (A) was recrystallised from *cyclo*hexane. The m. p.s of various specimens were in the range 223—243°, only some of which were raised by recrystallisation from *cyclo*hexane, light petroleum (b. p. 100—120°), or light petroleum (b. p. 60—80°)–toluene [Found: C, 82·0; H, 6·1; N, 12·0; *C*-Me, 6·2%; *M*, 488 (±35). Calc. for $C_{32}H_{24}N_4$: C, 82·0; H, 6·0; N, 12·0; *C*-Me, 6·4%; *M*, 468]. Comparison of the infrared spectrum with those of various azophenines, whose preparation is described below, combined with the analytical data, show that (A) was a mixture of *p*-methylated azophenines.

*Quinone Dianil.*—A mixture of *NN′*-diphenyl-*p*-phenylenediamine (6·1 g.), yellow mercuric oxide (12·0 g.), and dry benzene (150 ml.) was stirred and heated under reflux for 8 hr., cooled, and filtered. The filtrate was evaporated and the residue, crystallised from ethanol, had m. p. 181·5—182·5° (5·28 g., 87%) (Bandrowski [11] gave m. p. 176—181°) (Found: C, 83·9; H, 5·6; N, 11·0. Calc. for $C_{18}H_{14}N_2$: C, 83·7; H, 5·5; N, 10·9%). Light absorption in 95% EtOH: $\lambda_{max.}$ 304, 443 (ε 26,800, 8000); $\lambda_{min.}$ 238, 360 mμ (6790, 2000). Infrared max.: 6·32s, 6·70s, 6·90s, 7·56w, 7·65w, 8·25w, 8·55w, 8·65w, 8·96w, 9·30m, 9·77w, 10·16w, 10·35w, 10·50m, 10·96m, 11·56m, 11·67s, 12·76s, 13·35w, 13·76s, and 14·35 μ s (s = strong, m = medium, w = weak here and below).

p-*Benzoquinone Di-*p*-tolylimine.*—*NN′*-Di-*p*-tolyl-*p*-phenylenediamine was prepared by the method of Hatschek and Zega.[12] The product (40—60% yield), recrystallised from benzene, had m. p. 181°. Oxidation with yellow mercuric oxide gave the *di-*p*-tolylimine* as red needles (from ethanol), m. p. 123—123·5° (94%) (Found: C, 83·9; H, 6·7; N, 9·75. $C_{20}H_{18}N_2$ requires C, 83·9; H, 6·3; N, 9·8%). Light absorption in 95% ethanol: $\lambda_{max.}$ 310, 464 (ε 27,500, 11,600); $\lambda_{min.}$ 218, 240, 277, 368 (ε 11,900, 7800, 15,900, 2070); $\lambda_{infl.}$ 233, 270 mμ (ε 12,200, 16,200). Infrared max.: 6·35s, 6·67s, 7·60s, 8·24w, 9·06m, 9·60w, 9·87w, 10·15w, 10·47m, 11·54m, 11·63s, 11·71s, 12·00s, 12·15s, 12·70m, 13·57m, and 14·35 μ m.

*Reaction of Benzoquinone Dianils with Aromatic Amines.*—The dianil was dissolved in the minimum of dilute acetic acid, and a large excess of the amine added. The mixture was heated on a water-bath for the stated time, cooled, and filtered. The residue was washed with hot ethanol and recrystallised from light petroleum (b. p. 100—120°). All azophenines crystallised as red needles. Products are recorded in the annexed Table.

| Reactants | Time (min.) | Azophenine produced | M. p. |
|---|---|---|---|
| *p*-Benzoquinone dianil + aniline | 5, 60 | Ia | 236—237° |
| ,, ,, *p*-toluidine | 5 | Ib | 233—235, 236 |
| ,, ,, ,, | 15 | Mixture Ib & c | 236—237 |
| ,, ,, ,, | 60 | ,, | 253 |
| *p*-Benzoquinone di-*p*-tolylimine + *p*-toluidine | 5, 60 | Ic | 264—265 |
| ,, ,, aniline | 5 | Ib | 234, 235 |
| ,, ,, ,, | 60 | Ia | 235·5, 235·5—236 |

*Properties of azophenines:* Azophenine, m. p. 236—237° (lit., between 225° and 250°) (Found: N, 12·6. Calc. for $C_{30}H_{24}N_4$: N, 12·7%). Light absorption in ether: $\lambda_{max.}$ 290, 384—388 (ε 33,900, 20,400); $\lambda_{min.}$ 250, 332 (ε 17,600, 10,800); $\lambda_{infl.}$ 400—404 mμ (18,300). Infrared max.: 3·05s, 6·27s, 6·44s, 6·65s, 6·75s, 6·92s, 7·44m, 7·74m, 8·05w, 8·30w, 8·56m, 8·66m, 9·30m, 9·80w, 10·65w, 10·97w, 11·51m, 11·76m, 11·87m, 12·07,m 12·83m, 13·05s, 13·28s, 13·61w, 13·99m, 14·15m, 14·40s, 14·71m, and 15·01 μ w.

Tetra-*p*-methylazophenine, m. p. 264—265° (lit., 249°,[13] 259—260° [14]) (Found: N, 11·35.

[10] Barsilowsky, *Annalen*, 1881, **207**, 103.
[11] Bandrowski, *Monatsh.*, 1886, **7**, 375.
[12] Hatschek and Zega, *J. prakt. Chem.*, 1886, **33**, 209.
[13] Fischer and Hepp, *Ber.*, 1887, **20**, 2480.
[14] Ruggli and Buchmeier, *Helv. Chim. Acta*, 1945, **28**, 850.

Calc. for $C_{24}H_{22}N_4$ : N, 11·3%). Light absorption in ether : $\lambda_{max.}$ 290, 395 (ε 33,000, 20,700); $\lambda_{min.}$ 244, 388 (ε 16,400, 8700); $\lambda_{infl.}$ 222—227, 398—404 mμ (ε 23,100, 20,400). Infrared max. : 3·02s, 6·27s, 6·45s, 6·72s, 7·47s, 7·71m, 8·09w, 8·25w, 8·34w, 8·55w, 9·03w, 9·83w, 10·57w, 11·70m, 12·17s, 12·35s, 12·78w, 13·15s, 13·70s, 13·93w, and 14·10 μ m.

Di-*p*-methylazophenine, m. p. 236°. Light absorption in ether : $\lambda_{max.}$ 290, 388—390(ε 29,800, 18,700); $\lambda_{min.}$ 252, 336 mμ (ε 15,500, 8100). Infrared max. : 3·05 μ (N–H) and (in the 11—15 μ region) 11·03w, 11·47w, 11·67m, 11·81m, 12·33s, 12·87m, 13·15m, 13·98m, 14·40s, and 14·83 μ w. The maximum at 3·05 μ strongly suggests that the compound is 2 : 5-dianilino-*p*-benzoquinone di-*p*-tolylimine.

*Reaction between the Di-*p*-methylazophenine and* p-*Toluidine.*—The azophenine (61 mg.) was dissolved in dimethylformamide (100 ml.), and *p*-toluidine (2 g.) and acetic acid (5 ml.) were added. The solution was heated on a water-bath for 3 hr., then concentrated to 5 ml. Ethanol (20 ml.) was added and the red crystals were filtered off, dried (56 mg.), and recrystallised from benzene–light petroleum (b. p. 100—120°) as red needles, m. p. 227—232°. These were dissolved in dimethylformamide (150 ml.), and *p*-toluidine (2 g.) and acetic acid (10 ml.) were added. After being heated at 100° for 18 hr., the product was isolated as above as red needles (30 mg.), m. p. 259—260°, mixed m. p. with tetra-*p*-methylazophenine, 263—264°.

*Identification of Substance* (B).—The compound (B) was obtained as red needles, m. p. 211—212° (150 mg.). Recrystallisation from either *cyclo*hexane or ethanol–chloroform raised the m. p. to 215—217°. In concentrated sulphuric acid, compound (B) gave a blue-red solution, unaltered on being heated [Found : C, 79·4; H, 5·8; N, 11·2%; *M* (Rast), 370 (±30). Calc. for $C_{25}H_{21}ON_3$ : C, 79·1; H, 5·6; N, 11·1%; *M*, 379. Calc. for $C_{24}H_{19}ON_3$ : C, 78·9; H, 5·1; N, 11·5%; *M*, 365].

These facts suggest that (B) was 2-hydroxy-5-*p*-toluidino-*p*-benzoquinone dianil ($C_{25}H_{21}ON_3$), which we synthesised by the method of Heller,[15] who gave m. p. 214°.

Crude 4-hydroxy-4′-methyldiphenylamine was oxidised to *p*-benzoquinone mono-*p*-tolylimine, red needles [from light petroleum (b. p. 40—60°)], m. p. 81° (Found : N, 7·3. Calc. for $C_{13}H_{11}ON$ : N, 7·1%). Infrared max. : 5·21w, 6·09s, 6·17s, 6·35m, 6·67m, 7·07w, 7·60s, 7·66m, 7·99w, 8·28w, 8·53m, 8·63m, 9·04w, 9·63w, 10·17w, 10·31w, 10·53m, 11·52s, 11·99s, 12·66w, 12·95w, 13·14m, 13·50w, and 14·23 μ m.

*p*-Benzoquinone mono-*p*-tolylimine reacted with aniline, to give 2-hydroxy-5-*p*-toluidino-*p*-benzoquinone dianil, m. p. 213°, mixed m. p. with specimen from peroxidase action, 214° (Found : N, 10·7%). Light absorption in ether : $\lambda_{max.}$ 289, 387 (ε 35,150, 19,800); $\lambda_{min.}$ 251, 338 (ε 30,250, 12,500); $\lambda_{infl.}$ 265 mμ (ε 31,600). Infrared max. : 3·05s, 6·26s, 6·40s, 6·60s, 7·45s, 7·69s, 8·08m, 8·33m, 8·55m, 9·01w, 9·34w, 9·75w, 9·85w, 10·60w, 11·05w, 11·69m, 11·08m, 12·17s, 12·28s, 12·85m, 13·15m, 13·97m, and 14·37 μ s.

*Identification of Substance* (C).—Crude (C), m. p. 157—162° (632 mg.), was purified by chromatography on alumina in benzene. The eluate from the main band was evaporated to a red glass which crystallised on addition of *cyclo*hexane (15 ml.). The crystals (400 mg.) had m. p. 173—174°, unaltered on recrystallisation from either *cyclo*hexane or ethanol–chloroform (Found : C, 79·6; H, 6·0; N, 14·7; *C*-Me, 4·7. $C_{25}H_{22}N_4$ requires C, 79·4; H, 5·8; N, 14·8; *C*-Me, 4·0%). Light absorption in ether : $\lambda_{max.}$ 228, 279, 356 (ε 28,000, 22,600, 19,900); $\lambda_{min.}$ 222, 252, 320 mμ (ε 20,900, 16,100, 8970). Infrared max. : 2·89m, 3·025s, 6·24s, 6·43s, 6·60s, 6·68s, 7·42s, 7·54m, 7·88m, 8·10s, 8·30s, 8·47m, 8·61w, 9·01w, 9·35w, 9·76w, 9·84w, 10·65w, 10·87w, 11·15w, 11·69m, 11·90m, 12·10s, 12·15m, 12·90m, 13·00m, 13·85m, 14·13m, 14·45s, and 14·99 μ w.

Substance (C) gave a magenta solution in concentrated sulphuric acid, which became red on dilution, blue-violet on heating, and on more prolonged heating blue-black. Both blue solutions became red on dilution and fluoresced slightly.

The above suggested that (C) was a homologue of 2-amino-5-anilino-*p*-benzoquinone dianil and was shown to be a compound of this type by acetylation and by reaction with *p*-toluidine.

The compound (73 mg.) was heated under reflux with acetic anhydride (2 ml.) for 10 min., the mixture cooled, ethanol (5 ml.) added, and the mixture filtered. The red residue of 2-*acetamido*-5-p-*toluidino*-p-*benzoquinone dianil* recrystallised from ethanol as scarlet needles, m. p. 174—176° (Found : N, 13·1. $C_{27}H_{24}ON_4$ requires N, 13·3%).

The compound (C) (111 mg.), *p*-toluidine (0·25 g.), water (12·5 ml.), and acetic acid (12·5 ml.) were heated together on a water-bath for 2 hr. The red amorphous precipitate was filtered off, washed, dried (m. p. 226—227°), and recrystallised from toluene–light petroleum (b. p. 80—100°)

[15] Heller, *Annalen*, 1919, **418**, 265.

as red needles, m. p. 233—234° (Found: *C*-Me, 6·6. Calc. for $C_{32}H_{24}N_4$: 2*C*-Me, 6·4%). Infrared max. in the 11—15 μ region: 11·69m, 11·80w, 12·15s, 12·30m, 12·85w, 13·15w, 13·75s, 14·10s, 14·37m, and 14·85 μ w. This spectrum is similar to that of the fourth product in the Table, which had max. at 11·49w, 11·70m, 12·15s, 12·34m, 13·92w, 14·10m, and 14·37 μ w, *i.e.*, the above product is a mixture.

2-*Amino*-5-*anilino*-p-*benzoquinone Dianil*.[16]—To a stirred solution of aniline (60 g.) in water (1·2 l.) and glacial acetic acid (40 g.), at 0°, lead dioxide (160 g.) was added portionwise during 0·5 hr. The mixture was filtered, and the residue extracted with cold benzene (1 l.) and filtered. This filtrate was passed through a column of alumina (6·5 × 11·0 cm.), and the eluate concentrated to 300 ml. The concentrate was chromatographed on alumina in benzene containing ethanol (2%). The main band was preceded by a small quantity of azobenzene. The eluate containing the main band was evaporated, to yield a dark red amorphous residue, which was recrystallised from ethanol–chloroform. The first crop of crystals had m. p. 163—164° (2·3 g.) (Found: C, 78·7; H, 5·7. Calc. for $C_{24}H_{20}N_4$: C, 79·1; H, 5·5%). Light absorption in ether: $\lambda_{max.}$ 228, 277, 356 (ε 24,400, 22,000, 21,900); $\lambda_{min.}$ 256, 316 (ε 19,500, 9370); $\lambda_{infl.}$ 240—244 mμ (ε 21,950). Infrared max.: 2·87s, 2·97s, 3·035s, 6·17s, 6·26s, 6·40s, 6·57s, 6·67m, 6·74s, 7·35m, 7·40m, 7·55m, 7·65m, 7·83w, 7·87w, 8·10m, 8·25m, 8·57w, 8·67w, 9·35m, 9·76m, 10·95w, 11·14w, 11·65w, 12·17s, 12·67w, 12·80s, 12·92m, 13·15s, 14·30s, 14·40s, and 14·98 μ w.

p-*Nitro*-N-p-*tolylaniline*.—*p*-Bromotoluene (56 g.), *p*-nitroaniline (20 g.), potassium carbonate (10 g.), copper powder (0·2 g.), and potassium iodide (0·5 g.) were heated together under reflux, with stirring, for 14 hr. The mixture was then steam-distilled to remove unchanged *p*-bromotoluene. The residue was filtered, the insoluble material was heated with 3N-hydrochloric acid (300 ml.) for 0·5 hr., and the mixture cooled and filtered. The residue (9·0 g.) was chromatographed on alumina in benzene to give two main bands (i) and (ii). Band (i), on evaporation, gave p-*nitro*-NN-*di*-p-*tolylaniline* (2·49 g., 5·5%) as yellow hexagonal plates, which on recrystallisation from ethanol–benzene, had m. p. 163·5—164·5° (Found: C, 75·4; H, 5·5; N, 8·6. $C_{20}H_{18}O_2N_2$ requires C, 75·5; H, 5·7; N, 8·8%). Band (ii), on evaporation, gave *p*-nitro-*N*-*p*-tolylaniline (7·04 g., 21%) as orange prisms, which on recrystallisation from dilute ethanol had m. p. 137° (Goldberg[17] gave m. p. 138°) (Found: C, 68·6; H, 5·4; N, 12·0. Calc. for $C_{13}H_{12}O_2N_2$: C, 68·4; H, 5·3; N, 12·3%).

N-*Toluene*-p-*sulphonyl*-N′-p-*tolyl*-p-*phenylenediamine*.—*N*-*p*-Tolyl-*p*-phenylenedianine[18] (713 mg.) was dissolved in pyridine (2 ml.), and a solution of toluene-*p*-sulphonyl chloride (700 mg.) in pyridine (4 ml.) added. The mixture was set aside for an hour, ethanol (2 ml.) added, and the mixture poured into water; the derivative crystallised. N-*Toluene*-p-*sulphonyl*-N′-p-*tolyl*-p-*phenylenediamine* recrystallised from dilute ethanol as leaflets, m. p. 163—165° (1·07 g., 85%) (Found: C, 68·3; H, 5·5; N, 8·2. $C_{20}H_{18}O_2N_2S$ requires C, 68·6; H, 5·2; N, 8·0%).

p-*Benzoquinone Imine* p-*Tolylimine*.—*N*-*p*-Tolyl-*p*-phenylenediamine was oxidised by silver oxide as described by Willstätter and Kubli.[19] The di-imine formed yellow crystals (from ether), m. p. 107—109° (Willstätter reported m. p. 114°) (Found: C, 79·8; H, 6·35; N, 14·4. Calc. for $C_{13}H_{12}N_2$: C, 79·6; H, 6·2; N, 14·3%). Light absorption in ether: $\lambda_{max.}$ 278, 434 (ε 18,500, 2870); $\lambda_{min.}$ 356 mμ (ε 930).

4-*Toluene*-p-*sulphonamidodiphenylamine*.—4-Aminodiphenylamine (8·4 g.) was treated with toluene-*p*-sulphonyl chloride (9·5 g.) as above. The *amide* recrystallised from dilute ethanol as rectangular plates, m. p. 145—145·5° (14·0 g., 91%) (Found: C, 67·2; H, 5·3; N, 8·4. $C_{19}H_{18}O_2N_2S$ requires C, 67·4; H, 5·4; N, 8·3%).

*Oxidation of* 4-*Toluene*-p-*sulphonamidodiphenylamine*.—The amide (451 mg.) was treated in dry benzene (300 ml.) with lead tetra-acetate (594 mg.), heated under reflux, with stirring, for 10 hr., cooled, and filtered, and the filtrate was evaporated. Addition of ether (5 ml.) and scratching caused the red *toluene*-p-*sulphonimido*-p-*benzoquinone anil* to crystallise. The ether was evaporated and the quinone collected (m. p. 93—95°; 400 mg., 89%); recrystallised from ether, it had m. p. 98° (Found: C, 67·9; H, 5·0; N, 8·3. $C_{19}H_{16}O_2N_2S$ requires C, 67·9; H, 4·8; N, 8·3%). Light absorption in ether: $\lambda_{max.}$ 223, 317, 480 (ε 14,600, 25,600, 4600); $\lambda_{min.}$ 240, 400 mμ (ε 6350, 1620). Infrared max.: 6·15m, 6·28w, 6·37s, 6·65s, 7·63s, 7·67s, 7·77s, 8·26w, 8·45w, 8·54m, 8·66s, 8·72s, 9·06m, 9·20s, 9·80m, 10·02w, 10·45w, 10·87w, 11·50s, 11·72s, 11·83s, 11·93m, 12·30m, 12·51s, 13·01w, 13·19w, 13·97s, 14·30s, and 14·79 μ s.

[16] Improvement on the method of Majima and Aoki, *Ber.*, 1911, **44**, 3080.
[17] Goldberg, G.P. 1906, 185,663, *Chem. Zentr.*, 1907, II, 957.
[18] Ullmann and Dahmen, *Ber.*, 1908, **41**, 3751.
[19] Willstätter and Kubli, *Ber.*, 1909, **42**, 4135.

The identity of the quinone was also established by reduction. Toluene-*p*-sulphonimido-*p*-benzoquinone anil (20 mg.) was shaken in ether (3 ml.) with sodium dithionite (50 mg.) in water (3 ml.). The ether layer was washed with water, dried ($Na_2SO_4$), and evaporated. The residue, recrystallised from dilute ethanol, had m. p. and mixed m. p. with 4-toluene-*p*-sulphonamidodiphenylamine, 145°.

*Reaction of* p-*Benzoquinone Toluene*-p-*sulphonimide Anil with Aniline.*—The anil (30 mg.) in dioxan (5 ml.) was warmed with a solution of aniline (1 ml.) in acetic acid (1 ml.) for 5 min., water (20 ml.) was added, and the mixture filtered. The red residue was washed with water, cold ethanol, and hot ethanol, giving, in each case, colourless washings. The residue, m. p. 225—235°, recrystallised from light petroleum (b. p. 100—120°) as red needles, m. p. and mixed m. p. with azophenine, 236°.

*Reaction of the Above Anil with* p-*Bromoaniline.*—The anil (128 mg.) was treated as above, the aniline being replaced by *p*-bromoaniline. *Tri*-p-*bromoazophenine* was obtained as red needles, m. p. 232—236° (Found: Br, 36·6. $C_{30}H_{21}N_4Br_3$ requires Br, 35·4%).

*Examination of Fraction* ii (p. 3816).—Fraction ii (5·68 g.) was chromatographed on alumina (7 × 40 cm.) in benzene. The lowest band, on evaporation, gave red needles, m. p. 229—233° (143 mg.). An infrared spectrum showed that this substance was a mixture of *p*-methylated azophenines.

It was not possible to separate the remaining bands either by silica or alumina chromatography.

One of us (G. M. K. H.) is indebted to the D.S.I.R. for a maintenance allowance. We are grateful to Dr. V. M. Clark with whom we have had valuable discussions.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, May 14th*, 1956.]

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## 742. *Synthetic and Oxidative Studies in the Polyhydroxydiphenyl Series. Part II.*[1] *5 : 6-Dichloro-2 : 3-dihydroxydiphenyl.*

By J. MALCOLM BRUCE and F. K. SUTCLIFFE.

Nitration of 4 : 5-dichloroveratrole yields the 3-nitro-derivative, and this has been converted into 4 : 5-dichloro-3-iodoveratrole which, with iodobenzene and copper, affords both 5 : 6-dichloro-2 : 3-dimethoxy- and 5 : 6 : 5′ : 6′-tetrachloro-2 : 3 : 2′ : 3′-tetramethoxy-diphenyl. However, the former diphenyl is more conveniently prepared by treatment of 2 : 3-dimethoxydiphenyl[1] with sulphuryl chloride. It is readily demethylated, and the resulting dihydric phenol is converted by mild oxidants into the corresponding diphenoquinone.

IN Part I [1] the preparation, from 3-lithioveratrole and *cyclo*hexanone, of 2 : 3-dihydroxydiphenyl was described. On oxidation in anhydrous solution this yielded 2 : 3-diphenoquinone, but in aqueous media dark amorphous products were formed, most probably by polymerisation involving the 5- and the 6-position. In order to investigate the possibility of ring fission in 2 : 3-diphenoquinones it is necessary to suppress this polymerisation by the introduction of blocking groups, and in the present paper the synthesis of 5 : 6-dichloro-2 : 3-dihydroxydiphenyl is described.

4 : 5-Dichloroveratrole (I) was prepared by chlorination of veratrole with an excess of sulphuryl chloride; even after prolonged refluxing, the dichloro-compound is the sole product. Peratoner and Ortoleva [2] have reported the preparation of this compound by use of exactly two equivalents of chlorinating agent.

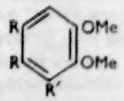
In an attempt to prepare 4 : 5-dichloro-3-lithioveratrole, the compound (I) was treated in ethereal solution with one equivalent of *n*-butyl- and phenyl-lithium severally, and the resulting mixtures were carboxylated. No pure product was isolated from the former reaction, but phenyl-lithium afforded, probably, 4 : 5-diphenylveratrole (II). This

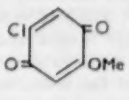
[1] Part I, Bruce and Sutcliffe, *J.*, 1955, 4435. Throughout this paper, "diphenylbenzoquinone," wherever it occurs, should read "diphenoquinone."
[2] Peratoner and Ortoleva, *Gazzetta*, 1898, **28**, I, 232.
[3] Wittig and Fuhrmann, *Ber.*, 1940, **73**, 1197.

structure is supported by the ultraviolet absorption spectrum and by an analogous reaction of 3-chloroanisole, giving 3-methoxydiphenyl, described by Wittig and Fuhrmann.[3]

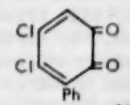
In view of these results, alternative routes to the dichlorodimethoxydiphenyl (III) were sought. Nitration of 4 : 5-dichloroveratrole afforded the 3-nitro-derivative, m. p. 111·5°, together with the quinone (IV); Cousin [4] prepared *x* : *y*-dichloro-3-nitroveratrole, m. p.

(I) R = Cl, R′ = H
(II) R = Ph, R′ = H
(III) R = Cl, R′ = Ph





(IV)



(V)

110—111°, by chlorination of 3-nitroveratrole, and the present work indicates that his product was the 5 : 6-dichloro-isomer. Reduction of 4 : 5-dichloro-3-nitroveratrole yielded the corresponding amine, which was converted *via* the diazonium chloride into 4 : 5-dichloro-3-iodoveratrole. The latter, with iodobenzene and copper in the Ullmann reaction, afforded both the required diphenyl (III) and 5 : 6 : 5′ : 6′-tetrachloro-2 : 3 : 2′ : 3′-tetramethoxydiphenyl.

5 : 6-Dichloro-2 : 3-dimethoxydiphenyl was more conveniently prepared by refluxing 2 : 3-dimethoxydiphenyl [1] with a large excess of sulphuryl chloride. On being demethylated it gave the corresponding dihydroxydiphenyl, which with silver oxide in ether afforded 5 : 6-dichloro-2 : 3-diphenoquinone (V). This quinone was also obtained by effecting the oxidation with sodium iodate in aqueous media, from which it separated in an anhydrous state.

5 : 6-Dichloro-2 : 3-diphenoquinone is more soluble in organic solvents than is the parent 2 : 3-diphenoquinone [1] and, as expected, it is also much more stable. Thus it remains unchanged for several hours at 20° in 2% aqueous sodium carbonate, sodium hydrogen carbonate, or disodium hydrogen phosphate; 2 : 3-diphenoquinone dissolved to a brown solution. At 100°, dichlorodiphenoquinone dissolves completely. Both quinones are rapidly decomposed by cold 2% aqueous sodium hydroxide.

## Experimental

Reactions with organolithium compounds were carried out under oxygen-free nitrogen. Sulphuryl chloride was distilled through a short Dufton column immediately before use and had b. p. 68·5°. Solutions in organic solvents were dried with sodium sulphate. Absorption spectra were measured in dioxan in a Unicam S.P. 500 spectrophotometer. M. p.s are corrected.

4 : 5-*Dichloroveratrole* (I).—Sulphuryl chloride (284 c.c.) was added during 1 hr. to stirred veratrole (207 g.) at 15—20°, and stirring was continued at this temperature for 1 hr. and then at 75—80° for 2 hr. The excess of chloride was removed at 30 mm. and the residue, after being washed with a little cold light petroleum (b. p. 40—60°), was crystallised from ethanol, to give dichloroveratrole (249 g., 80%) as needles, m. p. 83·5° (Peratoner and Ortoleva [5] report m. p. 85·5—86·5°) (Found : Cl, 34·2. Calc. for $C_8H_8O_2Cl_2$ : Cl, 34·3%).

4 : 5-*Diphenylveratrole* (II).—Phenyl-lithium, from bromobenzene (9 g.) and lithium (0·9 g.), in ether (35 c.c.) was stirred at 0° whilst 4 : 5-dichloroveratrole (8·3 g.) in ether (80 c.c.) was added during 30 min. After being stirred at 20° for 2½ hr. the brown suspension was added to solid carbon dioxide (75 g.), the mixture was decomposed with water, and the ethereal phase was separated, washed with water, and dried; acidification of the aqueous phase failed to yield a precipitate. Removal of the ether and distillation of the residue gave a fore-run of dichloroveratrole (1·1 g.) and then a yellow viscous oil, b. p. 180—210°/0·3 mm., from which, by trituration with cold light petroleum (40 c.c.; b. p. 60—80°), a solid (1·4 g.) was obtained. Crystallisation of this from ethanol gave 4 : 5-*diphenylveratrole* as rhombic plates, m. p. 147° (Found : C, 82·7; H, 6·1. $C_{20}H_{18}O_2$ requires C, 82·8; H, 6·2%). Light absorption : $\lambda_{max.}$ 238, 283 mμ (log ε 4·43, 4·09). 1 : 2-Diphenylbenzene has $\lambda_{max.}$ 232 mμ (log ε 4·44).

In an experiment with ethereal *n*-butyl-lithium, an acidic fraction was obtained, but no pure material could be isolated from it.

4 : 5-*Dichloro-3-nitroveratrole*.—Nitric acid (305 c.c., *d* 1·45) was cooled to 0° and added to

[4] Cousin, *Compt. rend.*, 1902, **135**, 969; *Ann. Chim. Phys.*, 1903, **29**, 87.

stirred, freshly distilled, acetic anhydride (560 c.c.) at >5° (ice–salt). **4 : 5-Dichloroveratrole** (166 g.) was added with stirring at 0—2° during 40 min., stirring was continued for 30 min., and the yellow suspension was poured on ice (8 kg.). After being kept overnight, the solid was collected, washed with water, and extracted at 20° with benzene (1·5 l.); sublimation of the insoluble material (26·5 g., 20%) at 180°/25 mm. and crystallisation of the sublimate from butan-1-ol afforded **2-chloro-5-methoxy-1 : 4-benzoquinone** as bright yellow needles, m. p. 175·5° (lit.,[5] 172°, 172—173°, 173°) (Found: C, 48·8; H, 2·9; Cl, 20·4. Calc. for $C_7H_5O_3Cl$: C, 48·7; H, 2·9; Cl, 20·6%). Light absorption: $\lambda_{max.}$ 270, 370 mμ (log ε 4·21, 2·76). The benzene extract was washed with 10% aqueous sodium hydroxide, then with water, dried, and concentrated to 500 c.c., and the solution was chromatographed on alumina (200 × 45 mm.). Elution with benzene, removal of the solvent, and crystallisation of the residue from benzene–light petroleum (b. p. 60—80°) afforded the *nitro-compound* (94 g., 47%) as almost colourless needles, m. p. 111·5° (Found: C, 38·3; H, 3·0; N, 5·5; Cl, 28·2. $C_8H_7O_4NCl_2$ requires C, 38·1; H, 2·8; N, 5·6; Cl, 28·2%).

*3-Amino-4 : 5-dichloroveratrole.*—**4 : 5-Dichloro-3-nitroveratrole** (88 g.), granulated tin (100 g.), acetic acid (250 c.c.), concentrated hydrochloric acid (380 c.c.), and water (380 c.c.) were heated together under reflux until a vigorous reaction set in. This was moderated by water-cooling, and, after 10 min., the mixture was refluxed for 30 min., cooled, and basified below 20° with 40% aqueous sodium hydroxide. The suspension was extracted with benzene, the extract was washed with water and dried, and the solvent was removed. Distillation of the residue gave an oil (65 g., 84%), b. p. 102°/0·25 mm., which solidified and, on crystallisation from light petroleum (b. p. 60—80°), afforded the stable *amine* as needles, m. p. 79° (Found: C, 43·6; H, 4·2; N, 6·5; Cl, 32·5. $C_8H_9O_2NCl_2$ requires C, 43·2; H, 4·1; N, 6·3; Cl, 32·0%). The *NN-diacetate* forms prisms [from benzene–light petroleum (b. p. 60—80°)], m. p. 119·5° (Found: C, 47·3; H, 4·3; N, 4·8; Cl, 23·3; Ac, 27·5. $C_{12}H_{13}O_4NCl_2$ requires C, 47·1; H, 4·3; N, 4·6; Cl, 23·2; Ac, 28·1%). The *β-naphthol azo-derivative* forms orange needles [from light petroleum (b. p. 100—120°)], m. p. 149° after sintering at 145° (Found: C, 57·4; H, 3·8; N, 7·7; Cl, 18·7. $C_{18}H_{14}O_3N_2Cl_2$ requires C, 57·3; H, 3·7; N, 7·4; Cl, 18·8%).

**4 : 5-Dichloro-3-iodoveratrole.**—3-Amino-4 : 5-dichloroveratrole (11·1 g.) in concentrated hydrochloric acid (50 c.c.) and water (125 c.c.) was diazotised at 0—5° with 20% aqueous sodium nitrite, and to the orange solution was added potassium iodide (11 g.) in water (25 c.c.). The suspension was kept at 20° for 30 min., and then heated on the boiling-water bath for 1 hr.; a dense brown oil separated. The aqueous phase was decanted, boiling water (250 c.c.) was added to the residue, and the mixture was basified with 10% aqueous sodium hydroxide. After cooling, the solid was extracted with benzene, and the extract was washed successively with 5% aqueous sodium hydroxide, water, 5% hydrochloric acid, and water, and dried. Removal of the solvent and distillation of the residue gave an oil, b. p. 107°/0·04 mm., which solidified and afforded the *iodo-compound* (12·4 g., 74%) as needles, m. p. 82·5°, from ethanol (Found: C, 28·7; H, 2·1; AgHal., 156. $C_8H_7O_2Cl_2I$ requires C, 28·8; H, 2·1; AgHal., 157%).

**5 : 6-Dichloro-2 : 3-dimethoxydiphenyl** (III).—(*a*) **4 : 5-Dichloro-3-iodoveratrole** (1·67 g.) and iodobenzene (2·5 g.) were stirred together at 225° whilst activated[6] copper bronze (4 g.) was added during 10 min. The temperature was kept for 15 min. at 225°, raised during 10 min. to 280°, kept for 20 min. at 280°, and was finally raised during 5 min. to 350°. The cooled mixture was repeatedly extracted with boiling light petroleum (b. p. 60—80°), the solvent was removed from the extract, and the residue was distilled to give: (1) a fore-run of iodobenzene; (2) a light yellow oil, b. p. 70—80°/0·05 mm., which solidified, and consisted mainly of diphenyl; (3) an oil, b. p. 115—120°/0·05 mm., which solidified and afforded *dichlorodimethoxydiphenyl* (0·27 g.) as rhombic plates, m. p. 89·5—90°, from light petroleum (b. p. 60—80°) (Found: C, 59·3; H, 4·0; Cl, 25·3. $C_{14}H_{12}O_2Cl_2$ requires C, 59·4; H, 4·2; Cl, 25·1%), light absorption: $\lambda_{max.}$ 292 mμ (log ε 3·36); (4) a yellow oil, b. p. 210°/0·02 mm., which solidified and was triturated with cold light petroleum (10 c.c., b. p. 40—60°); the insoluble solid (0·39 g.) was sublimed at 170°/0·03 mm. and the sublimate was crystallised from methanol, giving **5 : 6 : 5′ : 6′-tetrachloro-2 : 3 : 2′ : 3′-tetramethoxydiphenyl** as prisms, m. p. 172—172·5° (Found: C, 46·6; H, 3·2; Cl, 34·4. $C_{16}H_{14}O_4Cl_4$ requires C, 46·6; H, 3·4; Cl, 34·5%). Light absorption: $\lambda_{max.}$ 294 mμ (log ε 3·76).

(*b*) **2 : 3-Dimethoxydiphenyl**[1] (15·5 g.) was refluxed with sulphuryl chloride (135 c.c.) for 8 hr., the excess of chlorinating agent was removed, and the residue was dissolved in ether.

[5] Asp and Lindberg, *Acta Chem. Scand.*, 1950, **4**, 60; Ioffe and Sukhina, *Zhur. obshchei Khim.*, 1953, **23**, 295, 299.

[6] Kleiderer and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 4219.

The solution was washed with 10% aqueous sodium hydroxide, then water, and dried, and the solvent was removed. Distillation gave an oil, b. p. 115—135°/0·04 mm., from which, by crystallisation from light petroleum (b. p. 40—60°), 5 : 6-dichloro-2 : 3-dimethoxydiphenyl (15·1 g., 76%) was obtained as rhombic plates, m. p. 90° undepressed on admixture with material prepared by method (*a*) (Found : C, 59·1; H, 4·1; Cl, 24·9%).

5 : 6-*Dichloro*-2 : 3-*dihydroxydiphenyl*.—5 : 6-Dichloro-2 : 3-dimethoxydiphenyl (4·2 g.) was treated in dry chlorobenzene (100 c.c.) with powdered anhydrous aluminium chloride (7 g.), then refluxed for 3 hr., cooled, and poured into ice-cold 15% hydrochloric acid (200 c.c.). The suspension was stirred for 30 min. and extracted with ether, and the extract was washed with water and dried. Removal of the solvent left a dark solid which was washed with light petroleum (b. p. 40—60°) and sublimed at 150°/0·05 mm., to give a colourless microcrystalline powder (3·25 g., 85%); recrystallisation from light petroleum (b. p. 80—100°) afforded the *dihydroxydiphenyl* as needles, m. p. 150·5° (Found : C, 56·6; H, 3·1; Cl, 27·4. $C_{12}H_8O_2Cl_2$ requires C, 56·5; H, 3·1; Cl, 27·9%). Light absorption : $\lambda_{max.}$ 292 mμ (log ε 3·36) {*diacetate*, rhombic plates [from light petroleum (b. p. 40—60°)], m. p. 76·5° (Found : C, 56·9; H, 3·7; Cl, 20·7; Ac, 25·6. $C_{16}H_{12}O_4Cl_2$ requires C, 56·6; H, 3·5; Cl, 20·9; Ac, 25·4%)}.

5 : 6-*Dichloro*-2 : 3-*diphenoquinone* (V).—(*a*) Silver oxide, prepared [7] from silver nitrate (1 g.), and anhydrous sodium sulphate (2 g.) were suspended in dry ether (25 c.c.), and a solution of 5 : 6-dichloro-2 : 3-dihydroxydiphenyl (0·26 g.) in ether (25 c.c.) was added all at once. After 15 minutes' shaking at 20° the mixture was filtered, the red filtrate was concentrated, at 0°/20 mm., to 10 c.c. and cooled to −75°; the *quinone* (0·15 g., 60%) separated as a red microcrystalline powder, m. p. 127—129° (Found : C, 56·7; H, 2·7; Cl, 27·5. $C_{12}H_6O_2Cl_2$ requires C, 56·9; H, 2·4; Cl, 28·1%). Light absorption : $\lambda_{max.}$ 415 mμ (log ε 3·34).

(*b*) To 5 : 6-dichloro-2 : 3-dihydroxydiphenyl (128 mg.) in ethanol (10 c.c.) and water (5 c.c.) at 20° was added, all at once, sodium iodate hydrate (220 mg.) in water–ethanol (10 c.c., 5 c.c.). After 1½ hours' stirring at 20° the precipitate was collected, washed with 50% aqueous ethanol, then water, and dried *in vacuo*. The quinone (94 mg., 75%) was obtained as an orange-brown amorphous powder, m. p. 111—117°. Light absorption : $\lambda_{max.}$ 233, 395, 408 mμ (log ε 4·22, 3·35, 3·36). The mother-liquors, after dilution with water (20 c.c.), gradually deposited deep red platelets (9 mg.), m. p. 127—129° undepressed on admixture with the quinone prepared by method (*a*).

(*c*) The purest specimen of the quinone was obtained by oxidation of dichlorodihydroxydiphenyl (128 mg.) in dioxan (6·5 c.c.) and water (1·5 c.c.) with sodium iodate (55 mg.) in water (2 c.c.) at 20°. After 1 hour's stirring water (10 c.c.) was added, stirring was continued for 30 min., and the mixture was filtered from crude dichlorodiphenoquinone. The filtrate was diluted with water (5 c.c.) and set aside at 20° for several hours; the quinone (12 mg.) separated as deep red platelets with a golden reflex, m. p. 136—137° after sintering at 131°. Light absorption $\lambda_{max.}$ 224, 415 mμ (log ε 4·13, 3·38).

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[7] Willstätter and Müller, *Ber.*, 1908, **41**, 2581.

## 743. *Synthetic and Oxidative Studies in the Polyhydroxydiphenyl Series. Part III.*[1] 2 : 3-*Dihydroxy*-5 : 6-*dimethyldiphenyl.*

By J. Malcolm Bruce and F. K. Sutcliffe.

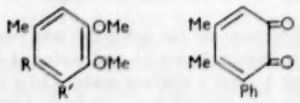
4 : 5-Dimethylveratrole has been prepared in 80% yield by a three-stage reaction from veratraldehyde, and also by treatment of 4 : 5-dichloroveratrole with methyl-lithium. With ethereal *n*-butyl-lithium it gives 13% of the 3-lithio-derivative which with carbon dioxide affords the corresponding carboxylic acid, but the expected tertiary alcohol was not obtained from reaction with *cyclo*hexanone. Ethereal 3-bromo-4 : 5-dimethylveratrole is largely debrominated by lithium or phenyl-lithium.

2 : 3-Dimethoxy-5 : 6-dimethyldiphenyl is formed in low yield by the crossed Ullmann reaction with 3-bromo-4 : 5-dimethylveratrole and iodobenzene. It is readily demethylated, and the resulting dihydric phenol is converted by mild oxidants into the corresponding diphenoquinone.

In Part II [1] it was shown that 4 : 5-dichloroveratrole could not be satisfactorily metallated owing to interaction of the halogen atoms with the organolithium compound, but such a reaction is precluded in 4 : 5-dimethylveratrole and it was hoped to prepare 2 : 3-dihydroxy-5 : 6-dimethyldiphenyl from this by a series of reactions analogous to those described in Part I.[2] The results of this work are described in the present paper.

4 : 5-Dimethylveratrole (I) was unknown until 1943, when Karrer and Schick [3] prepared it in an overall yield of 34% by the route: veratraldehyde ⟶ 4-methylveratrole ⟶ 6-methylveratraldehyde ⟶ (I). The aldehydes were reduced by catalytic hydrogenation of their anils, and it was at these stages that poor yields were obtained. Consequently, other methods of effecting the change R·CHO ⟶ R·$CH_3$ were examined, and the Huang-

(I) R = Me, R′ = H
(II) R = Me, R′ = $CO_2H$
(III) R = $CH_2·CO_2H$, R′ = H
(IV) R = Me, R′ = $NH_2$
(V) R = Me, R′ = Ph




(VI)

Minlon [4] modification of the Wolff–Kishner reduction was found to give excellent yields at both stages. 4-Methylveratrole was converted into 6-methylveratraldehyde by the modified [5] Gattermann reaction, this procedure being superior to formylation [6] with *NN*-dimethylformamide–phosphorus oxychloride mixture. 4 : 5-Dimethylveratrole is also formed when 4 : 5-dichloroveratrole reacts with ethereal methyl-lithium, this being analogous to the formation of 4 : 5-diphenylveratrole described in Part II.[1]

Reaction of 4 : 5-dimethylveratrole with one equivalent of ethereal *n*-butyl-lithium and subsequent carboxylation afforded 13% of 4 : 5-dimethylveratrole-3-carboxylic acid (II), m. p. 120°, and 13% of 4 : 5-dimethylguaiacol; with two equivalents of butyl-lithium the yields were 15% and 32% respectively. The carboxylic acid obtained from this reaction could have been [7] the isomeric phenylacetic acid (III), but this was synthesised by Sugasawa and Sigehara [8] and had m. p. 102—104°. Further confirmation of the orientation (II) was obtained by Schmidt degradation to 3-amino-4 : 5-dimethylveratrole (IV).

The expected tertiary alcohol could not be isolated after reaction of *cyclo*hexanone with metallated 4 : 5-dimethylveratrole, the main product being an oil which

[1] Part II, Bruce and Sutcliffe, preceding paper.
[2] *Idem*, *J.*, 1955, 4435.
[3] Karrer and Schick, *Helv. Chim. Acta*, 1943, **26**, 800.
[4] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.
[5] Adams and Levine, *ibid.*, 1923, **45**, 2373.
[6] Cf. Bau-Hoï and Lavit, *J.*, 1955, 2776.
[7] Cf. Letsinger and Schnizer, *J. Org. Chem.*, 1951, **16**, 869.
[8] Sugasawa and Sigehara, *Ber.*, 1941, **74**, 459.

on dehydration afforded a neutral compound $(C_{15}H_{20}O_2)_n$, m. p. 61·5°. Treatment of this with hydrobromic acid gave 4 : 5-dimethylcatechol, and it seemed possible that it was 4 : 5-dimethylguaiacol *cyclo*hexyl ether, $C_{15}H_{22}O_2$, but this was synthesised from 4 : 5-dimethylguaiacol and had m. p. 33°.

The failure of 3-lithio-4 : 5-dimethylveratrole to react in the expected manner with *cyclo*hexanone may be due to steric hindrance, though the low concentration of the lithio-compound could also be a contributing factor, and consequently attempts were made to prepare lithiodimethylveratrole by reactions involving halogen–metal interchange.

3-Iodo-4 : 5-dimethylveratrole could only be obtained from the amine (IV) from which the 3-bromo- and the 3-chloro-derivative were also prepared. The 3-bromo-compound was, however, more conveniently obtained by treatment of 4 : 5-dimethylveratrole with one equivalent of bromine; with two equivalents in the presence of a halogen carrier, 3 : 6-dibromo-4 : 5-dimethylveratrole was formed.

Reaction of 3-bromo-4 : 5-dimethylveratrole with one equivalent of ethereal phenyl-lithium and subsequent carboxylation afforded, unexpectedly, 78% of 4 : 5-dimethyl-veratrole and an unidentified carboxylic acid. When an ethereal solution of the bromo-compound was refluxed with lithium metal and then carboxylated, the products were 4 : 5-dimethylveratrole, 4 : 5-dimethylveratrole-3-carboxylic acid, and 4 : 5-dimethyl-guaiacol. No reaction occurred in benzene solution, nor did the compound react with magnesium. With two equivalents of ethereal phenyl-lithium, and subsequent carboxyl-ation, 3 : 6-dibromo-4 : 5-dimethylveratrole also suffered debromination, giving the acid (II); with lithium metal, only a trace of acidic material was formed, the main product being 3-bromo-4 : 5-dimethylveratrole.

Owing to the failure to obtain good yields of 3-lithio-4 : 5-dimethylveratrole, the Ullmann reaction with a mixture of 3-bromo-4 : 5-dimethylveratrole and iodobenzene was attempted, and this afforded the required diphenyl (V) in low yield, together with 2 : 3 : 2′ : 3′-tetramethoxy-5 : 6 : 5′ : 6′-tetramethyldiphenyl. An attempt was made to prepare dimethoxydimethyldiphenyl (V) by the reaction of 4 : 5-dichloro-3-phenyl-veratrole [1] with two equivalents of ethereal methyl-lithium, but, in contrast to 4 : 5-di-chloroveratrole itself, only one chlorine atom was replaced. The orientation of the product is being investigated. When the reaction was conducted in higher-boiling solvents the diphenyl suffered extensive decomposition.

2 : 3-Dihydroxy-5 : 6-dimethyldiphenyl was obtained by demethylation of its dimethyl ether (V), and on oxidation with silver oxide in ether or sodium iodate in aqueous ethanol it afforded 5 : 6-dimethyl-2 : 3-diphenoquinone (VI), which showed similar solubility properties to those of the parent 2 : 3-diphenoquinone.[2] The quinone was obtained by iodate oxidation as an amorphous powder which, in contrast to 5 : 6-dichloro-2 : 3-dipheno-quinone,[1] adsorbed considerable quantities of water. Like the dichlorodiphenoquinone, the compound (VI) is unaffected by long storage at 20° with 2% aqueous sodium carb-onate, sodium hydrogen carbonate, or disodium hydrogen phosphate, but when boiled with these aqueous bases it forms a dark mass which dissolves only partially. It is readily soluble, with decomposition, in 2% aqueous sodium hydroxide.

These differences between 5 : 6-dichloro- and 5 : 6-dimethyl-2 : 3-diphenoquinone suggest that, in the presence of aqueous bases, the former decomposes smoothly to soluble products whereas the latter both decomposes and polymerises. Such a polymerisation may be due to activation of the 4-position by the adjacent methyl group, or to participation of methyl groups in a chain-forming process. The marked instability of tetramethyl-1 : 2-benzoquinone [9] supports the second view.

## Experimental

Reactions with organolithium compounds were conducted under oxygen-free nitrogen. Solutions in organic solvents were dried with sodium sulphate. The term (c) indicates that crystallisation was effected by cooling of the solution, prepared at room temperature, in solid

[9] Smith and Hac, *J. Amer. Chem. Soc.*, 1934, **56**, 477.

carbon dioxide–acetone. Absorption spectra were measured in dioxan in a Unicam S.P. 500 spectrophotometer. M. p.s are corrected.

**4-*Methylveratrole*.**—Veratraldehyde (183 g.), potassium hydroxide pellets (200 g.), 90—95% hydrazine hydrate (145 c.c.), and diethylene glycol (1·4 l.) were heated under reflux (3 l. flask) on a boiling-water bath with frequent shaking until all the hydroxide had dissolved (30 min.); the aldehyde hydrazone separated as a pale yellow solid. The temperature (liquid) was then gradually raised. Decomposition of the hydrazone, indicated by evolution of nitrogen and considerable frothing, commenced at 95°, and during the subsequent heating regular shaking was necessary in order to break the foam; at 125° the froth rapidly subsided. After being refluxed (135°) for 3 hr. the solution was cooled and added to cold water (2·5 l.), and the oil was extracted with light petroleum (b. p. 60—80°). The extract was washed with 5% hydrochloric acid, then water and dried, and the solvent was removed. Distillation of the residue gave 4-methylveratrole (160 g., 96%), b. p. 60°/0·2 mm., m. p. 22·5° (Karrer and Schick [3] gave m. p. 21—22°).

**6-*Methylveratraldehyde*.**—(*a*) A rapid stream of dry hydrogen chloride was passed into a stirred mixture of powdered zinc cyanide (200 g.), 4-methylveratrole (160 g.), and dry benzene (1 l.) cooled in ice. After 3 hr., benzene (500 c.c.) and then, during 20 min., anhydrous aluminium chloride (175 g.) were added, and a slower passage of hydrogen chloride was continued at 0° for 20 min. and then at 40—45° for 1 hr. The mixture was cooled and added to ice-cold 10% hydrochloric acid (2·5 l.), and the suspension was stirred and refluxed for 1½ hr. After cooling, the benzene phase was separated, washed successively with water, 10% aqueous sodium hydroxide, and water, and dried. Removal of the solvent and distillation of the residue gave the aldehyde, b. p. 110—111°/0·2 mm., needles (158 g., 84%) [from benzene–light petroleum (b. p. 60—80°)], m. p. 74° (lit.,[3,10] 75°, 76°).

(*b*) Freshly distilled phosphorus oxychloride (41 c.c.) was added during 30 min. to a stirred mixture of 4-methylveratrole (53·5 g.) and *NN*-dimethylformamide (30 g., b. p. 151—152°). After being heated on the water-bath for 7 hr., the solution was poured into cold water (500 c.c.), an excess of 10% aqueous sodium hydroxide was added, and the solid which separated was extracted with benzene, the extract being washed with 5% hydrochloric acid and water, and dried. Removal of the solvent, distillation, and crystallisation as under (*a*) gave the aldehyde (41 g., 65%), m. p. 72—73°.

**4 : 5-*Dimethylveratrole* (I).**—(*a*) 6-Methylveratraldehyde (160 g.) was reduced with potassium hydroxide pellets (160 g.), 90—95% hydrazine hydrate (120 c.c.), and diethylene glycol (1·2 l.) as described for 4-methylveratrole; decomposition of the hydrazone commenced at 110°, but the foam did not subside until the reflux temperature (140°) was reached. Refluxing was continued for 3½ hr. 4 : 5-Dimethylveratrole (146 g., 99%), obtained by distillation, had b. p. 60°/0·2 mm., m. p. 42·5°. Crystallisation (c) from light petroleum (b. p. 40—60°) gave needles, m. p. 43° (Karrer and Schick [3] give m. p. 43·5°).

(*b*) To methyl-lithium, from methyl iodide (15·5 c.c.) and lithium (4 g.), in ether (150 c.c.) stirred at 0° was added during 45 min. 4 : 5-dichloroveratrole [1] (20·7 g.) in ether (150 c.c.), and the resulting grey suspension was stirred at 0° for 1 hr., at 20° for 1 hr. and then refluxed for 3 hr. After cooling, the mixture was decomposed at 0° with water (100 c.c.) and acidified with 10% hydrochloric acid, and the ethereal phase was separated, washed with water, and dried. Removal of the solvent and distillation of the dark residue gave a colourless oil, b. p. 58—60°/0·2 mm., from which, by crystallisation (c) from light petroleum (b. p. 40—60°), 4 : 5-dimethylveratrole (11 g., 66%) was obtained as needles, m. p. 40—41°.

**4 : 5-*Dimethylguaiacol and* 4 : 5-*Dimethylveratrole*-3-*carboxylic Acid* (II).**—*n*-Butyl-lithium, from *n*-butyl bromide (32 c.c.) and lithium (4·7 g.), in ether (150 c.c.) was added during 1 hr. to a stirred solution of 4 : 5-dimethylveratrole (40 g.) in ether (250 c.c.) at 0°, and stirring was continued at 0° for 1 hr. and then at 20° for 5 hr. The grey suspension was added to solid carbon dioxide (300 g.) and ether (100 c.c.), the mixture was decomposed with water (250 c.c.) and basified with 10% aqueous sodium hydroxide and the phases were separated. The ether solution, after being washed with water and dried, afforded, by distillation and crystallisation (c) of the distillate from light petroleum (b. p. 40—60°), 4 : 5-dimethylveratrole (17·5 g., 44%), m. p. 42° The aqueous phase was acidified at 10—15° with concentrated hydrochloric acid and extracted with ether. The extract was washed with water and dried, the solvent was removed and the residue distilled to give: (1) an oil, b. p. 48—50°/0·2 mm.; (2) a sublimate (bath-temp. 100°/0·2 mm.); and (3) a yellow viscous oil, b. p. 136°/0·15 mm., which solidified. Fractions (1) and (2) were combined and stirred with an excess of 5% aqueous sodium hydrogen

[10] Perkin and Weizmann, *J.*, 1906, **89**, 1649; Gattermann, *Annalen*, 1907, **357**, 370.

carbonate, and the solid (4·8 g., 13%) was collected and crystallised (c) from light petroleum (b. p. 40—60°) to give the *guaiacol* as blades, m. p. 68·5° (Found: C, 70·9; H, 7·7. $C_9H_{12}O_2$ requires C, 71·1; H, 7·9%). With dimethyl sulphate in aqueous sodium hydroxide, this afforded **4** : 5-dimethylveratrole, m. p. and mixed m. p. 43°, and on demethylation with 48% hydrobromic acid gave **4** : 5-dimethylcatechol (87%), needles [from light petroleum (b. p. 80—100°)], m. p. 86—87° undepressed on admixture with dimethylcatechol prepared [3] directly from **4** : 5-dimethylveratrole. Fraction (3) was extracted with 5% aqueous sodium hydrogen carbonate, the extract was slowly acidified at 10—15° with 10% hydrochloric acid, and the solid was collected, washed with water, and dried *in vacuo*; it had m. p. 61—66°, but, on being rubbed, the melt solidified and then had m. p. 116—118°. The anhydrous acid was obtained by refluxing this hydrate with light petroleum (b. p. 100—120°) under an azeotropic water-separator. Recrystallised from light petroleum (b. p. 80—100°), **4** : 5-*dimethylveratrole*-3-*carboxylic acid* (6·4 g., 13%) formed spikes, m. p. 120° (Found: C, 63·0; H, 6·6. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%).

3-*Amino*-**4** : 5-*dimethylveratrole* (IV).—Sodium azide (1·6 g.) was added during 30 min. to a stirred mixture of **4** : 5-dimethylveratrole-3-carboxylic acid (4·2 g.), chloroform (50 c.c.), and concentrated sulphuric acid (40 c.c.) at 20—21°. After 30 minutes' further stirring at this temperature the mixture was added to ice (150 g.), the chloroform layer was removed, and the aqueous phase was basified, below 20°, with 40% aqueous sodium hydroxide. The solid, separated by benzene extraction, gave, on distillation, the *amine* (3·4 g., 94%), b. p. 90°/0·1 mm., which solidified (m. p. 75°) and, on crystallisation (c) from light petroleum (b. p. 40—60°), afforded needles, m. p. 75·5° (Found: C, 66·3; H, 8·2; N, 7·8. $C_{10}H_{15}O_2N$ requires C, 66·3; H, 8·3; N, 7·7%). The β-*naphthol azo-derivative* formed red blades with a golden reflex (from butan-1-ol), m. p. 171° (Found: C, 71·3; H, 5·9; N, 8·5. $C_{20}H_{20}O_3N_2$ requires C, 71·4; H, 6·0; N, 8·3%).

*Reaction of Metallated* **4** : 5-*Dimethylveratrole with* cyclo*Hexanone*.—**4** : 5-Dimethylveratrole (50 g.) in ether (200 c.c.) was metallated, as described above, with *n*-butyl-lithium, from *n*-butyl bromide (42 c.c.) and lithium (6·2 g.) in ether (200 c.c.), and to the suspension was added at 0° during 1 hr. *cyclo*hexanone (51 c.c.) in ether (100 c.c.). After being stirred at 0° for 3 hr. and at 20° for 12 hr., the mixture was decomposed at 0° with water (250 c.c.) and acidified with concentrated hydrochloric acid. The ethereal phase was separated, washed with 5% aqueous sodium hydroxide (acidification of the washings gave 11·8 g. of dimethylguaiacol), then with water, and dried. Removal of the solvent and distillation of the residue gave: (1) a fore-run of *cyclo*hexanone; (2) an oil, b. p. 56—60°/0·2 mm., which, on crystallisation (c) from light petroleum (b. p. 40—60°), afforded dimethylveratrole (22 g.); and (3) a yellow viscous oil (11·1 g.), b. p. 130—132°/0·15 mm., from which no crystalline material could be obtained. Redistillation of the last gave: (4) an oil (0·4 g.), b. p. up to 129°/0·2 mm., which was discarded, (5) a yellow viscous oil (9·3 g.), b. p. 129—135°/0·2 mm., and (6) a yellow residue, which on trituration with light petroleum (b. p. 40—60°) gave a solid (33 mg.). Recrystallised from light petroleum (b. p. 100—120°) this formed needles, m. p. 186° (Found: C, 78·3; H, 10·1%). Fraction (5) was dehydrated by refluxing, under an azeotropic water-separator, for 30 min. with toluene (80 c.c.) and anhydrous oxalic acid (2 g.). The mixture was cooled and filtered, the filtrate was washed with water and dried, and the solvent was removed. Distillation of the residue afforded a yellow oil (7 g.), b. p. 126—129°/0·2 mm., which, on crystallisation (c) from light petroleum (b. p. 40—60°), gave a solid (3·9 g.); recrystallisation (c) from methanol afforded needles, m. p. 61·5° (Found: C, 77·5; H, 8·8%). On being refluxed for 6 hr. with 48% hydrobromic acid (25 c.c.), this compound (1 g.) yielded **4** : 5-dimethylcatechol (0·1 g.). The solvent was removed from the light petroleum mother-liquors, and the residue was dehydrogenated with chloranil (5 g.) in xylene (25 c.c.). After being refluxed for 8 hr., the solution was cooled and filtered from tetrachloroquinol, and the filtrate was washed with 10% aqueous sodium hydroxide, then water, and dried. Removal of the solvent and distillation gave a yellow oil, b. p. 106—134°/0·04 mm., which, on crystallisation (c) from light petroleum (b. p. 40—60°), afforded needles (60 mg.), m. p. 57·5—58·5° (Found: C, 78·4; H, 8·6%).

**4** : 5-*Dimethylguaiacol* cyclo*Hexyl Ether*.—**4** : 5-Dimethylguaiacol (6·1 g.) in ether (20 c.c.) and alcohol (20 c.c.) was added to a solution of sodium (1 g.) in ethanol (15 c.c.), the suspension was shaken for 20 min., and the sodium salt (5·5 g.) was collected, washed with ether, and dried *in vacuo*. A portion (1·8 g.), finely powdered, was stirred and refluxed for 150 hr. with *cyclo*hexyl bromide (1·5 c.c.) in dry xylene (50 c.c.), the suspension was cooled and filtered, and the filtrate was washed with 5% aqueous sodium hydroxide, then with water, and dried. Removal of the solvent and distillation gave a viscous oil, b. p. *ca.* 150°/0·03 mm., which, on crystallisation

(c) first from methanol and then from light petroleum (b. p. 40—60°), afforded the *ether* (0·35 g., 15%) as prisms, m. p. 33° (Found: C, 77·3; H, 9·3. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%).

3-*Iodo*-4 : 5-*dimethylveratrole*.—3-Amino-4 : 5-dimethylveratrole (0·72 g.) in concentrated hydrochloric acid (4 c.c.) and water (6 c.c.) was diazotised at 0° with 20% aqueous sodium nitrite, and to the orange solution was added potassium iodide (0·9 g.) in water (1 c.c.). After 1 hr. at 20° the mixture was heated on the water-bath until nitrogen evolution ceased and the *iodo-compound*, which separated as an oil, was worked up in the usual way. It had b. p. 90°/0·2 mm., and separated from methanol (c) as ill-defined crystals (0·7 g., 60%), m. p. 63·5° (Found: C, 41·4; H, 4·4; I, 43·4. $C_{10}H_{13}O_2I$ requires C, 41·1; H, 4·5; I, 43·5%).

3-*Chloro*-4 : 5-*dimethylveratrole*.—3-Amino-4 : 5-dimethylveratrole was diazotised as described for the preceding compound. Treatment of the solution with cuprous chloride and working up in the usual manner afforded the *chlorodimethylveratrole* (75%), b. p. 68°/0·15 mm., m. p. 21° (Found: C, 60·2; H, 6·7; Cl, 18·0. $C_{10}H_{13}O_2Cl$ requires C, 59·9; H, 6·5; Cl, 17·7%).

3-*Bromo*-4 : 5-*dimethylveratrole*.—(*a*) Diazotisation of 3-amino-4 : 5-dimethylveratrole (0·72 g.) in concentrated sulphuric acid (0·6 c.c.) and water (5 c.c.), treatment with cuprous bromide, and working up as usual gave the *bromodimethylveratrole*, b. p. 80°/0·2 mm., needles [from methanol (c)], m. p. 31° (Found: C, 49·2; H, 5·3; Br, 32·0. $C_{10}H_{13}O_2Br$ requires C, 49·0; H, 5·3; Br, 32·6%).

(*b*) Bromine (24 g.) in glacial acetic acid (150 c.c.) was added during 1¼ hr. to 4 : 5-dimethylveratrole (24·9 g.) in glacial acetic acid (150 c.c.) stirred at 10°. Stirring at 10° was continued for 45 min., and the solvent was then removed at 30—40°/20 mm. The residue, dissolved in light petroleum (b. p. 60—80°), was washed with 5% aqueous sodium hydroxide, with water, and dried, and the solvent was removed. Distillation of the residue gave an oil, b. p. 78—82°/0·15 mm., from which, by crystallisation (c) first from light petroleum (b. p. 40—60°) and then from methanol, the bromo-compound (24 g., 65%) was obtained as needles, m. p. 30·5° undepressed on admixture with material prepared by method (*a*) (Found: Br, 33·1%).

3 : 6-*Dibromo*-4 : 5-*dimethylveratrole*.—Bromine (16 g.) in glacial acetic acid (75 c.c.) was added during 30 min. to a stirred solution of 4 : 5-dimethylveratrole (8·3 g.) and iodine (0·2 g.) in glacial acetic acid (50 c.c.) at 20°. After being stirred at 20° for 5 hr. the mixture was worked up as described for the preceding compound, giving the *dibromodimethylveratrole* (10·7 g., 62%), b. p. 82—83°/0·03 mm., blades (from methanol), m. p. 79° (Found: C, 37·2; H, 3·6; Br, 48·9. $C_{10}H_{12}O_2Br_2$ requires C, 37·0; H, 3·7; Br, 49·4%).

*Reaction of* 3-*Bromo- and* 3 : 6-*Dibromo*-4 : 5-*dimethylveratrole with Phenyl-lithium*.—3-Bromo-4 : 5-dimethylveratrole (2·45 g.) in ether (20 c.c.) was added during 10 min. to a stirred solution of phenyl-lithium, from bromobenzene (2·3 g.) and lithium (0·2 g.), in ether (15 c.c.) stirred at 0°. After being stirred at 20° for 6 hr. the brown mixture was added to solid carbon dioxide (25 g.), water (50 c.c.) and 10% aqueous sodium hydroxide (20 c.c.) were added, and the phases were separated. The ethereal phase, after being washed with water and dried, afforded, by distillation, 4 : 5-dimethylveratrole (1·3 g., 78%), m. p. 41—42°. The aqueous phase was acidified with 10% hydrochloric acid, the liberated resin was taken up in ether, and the ethereal solution was extracted with 5% aqueous sodium hydrogen carbonate; acidification of this extract with 10% hydrochloric acid gave a resin, from which, by distillation and crystallisation of the distillate (b. p. *ca.* 180°/0·2 mm.) from light petroleum (b. p. 100—120°), a carboxylic acid (0·2 g.) was obtained as prisms, m. p. 168·5° (Found: C, 71·9; H, 6·3%).

When 3 : 6-dibromo-4 : 5-dimethylveratrole (3·24 g.) was similarly treated, with twice the quantity of phenyl-lithium, the products were: (1) a neutral compound which separated (c) from methanol as rhombic plates (30 mg.), m. p. 159—161° after sintering at 147° (Found: C, 87·6; H, 6·0%); (2) benzoic acid (0·5 g.); (3) 4 : 5-dimethylveratrole-3-carboxylic acid (0·25 g.), m. p. and mixed m. p. 119°; and (4) a carboxylic acid which crystallised from xylene as prisms (0·26 g.), m. p. 235—237° (Found: C, 59·6; H, 5·4%).

*Reaction of* 3-*Bromo- and* 3 : 6-*Dibromo*-4 : 5-*dimethylveratrole with Lithium*.—3-Bromo-4 : 5-dimethylveratrole (1·22 g.) in ether (10 c.c.) was refluxed with lithium wire (0·2 g.) for 3 hr., the suspension was cooled and filtered, and the filtrate was added to solid carbon dioxide (20 g.). The mixture was decomposed with water (25 c.c.), 10% aqueous sodium hydroxide (10 c.c.) was added, and the phases were separated and worked up as before, giving: (1) 4 : 5-dimethylveratrole (0·4 g., 48%), m. p. 41—42°; (2) 4 : 5-dimethylguaiacol (5 mg., 0·4%), m. p. 67—68°; and (3) 4 : 5-dimethylveratrole-3-carboxylic acid (35 mg., 3%), m. p. 118°.

Similar treatment of 3 : 6-dibromo-4 : 5-dimethylveratrole (1·62 g.) with lithium wire (0·4 g.) gave 3-bromo-4 : 5-dimethylveratrole (0·2 g., 17%), m. p. 29—30°; 0·3 g. (19%) of starting material was recovered.

In both cases, the lithium wire remained almost unchanged.

2 : 3-*Dimethoxy*-5 : 6-*dimethyldiphenyl* (V) *and* 2 : 3 : 2′ : 3′-*Tetramethoxy*-5 : 6 : 5′ : 6′-*tetramethyldiphenyl*.—3-Bromo-4 : 5-dimethylveratrole (1·22 g.) and iodobenzene (2·5 g.) were stirred together at 225° whilst activated [11] copper bronze (4 g.) was added during 10 min. The temperature was kept for 15 min. at 225°, raised during 10 min. to 280°, held for 20 min. at 280°, and finally raised during 5 min. to 350°. The cooled mixture was extracted with boiling light petroleum (b. p. 60—80°), the solvent was removed from the extract, and the residue was distilled giving: (1) a fore-run of iodobenzene; (2) an oil (0·85 g.), b. p. 70—72°/0·05 mm., which, crystallised from methanol, gave diphenyl; and (3) a yellow viscous oil (0·45 g.), b. p. 100—150°/0·05 mm., which largely solidified. This was triturated with cold light petroleum (3·5 c.c., b. p. 40—60°); the sparingly soluble solid (147 mg.) was collected [filtrate (A)] and crystallised from methanol, to give *tetramethoxytetramethyldiphenyl* as platelets, m. p. 133° (Found: C, 72·3; H, 7·7. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%). Light absorption: $\lambda_{max.}$ 284 mμ (log ε 3·65). The filtrate (A) was cooled to −75°, and the solid (65 mg.) was collected and crystallised (c) from light petroleum (b. p. 40—60°), to yield *dimethoxydimethyldiphenyl* as prisms, m. p. 64·5—65·5° (Found: C, 79·4; H, 7·4. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·4%). Light absorption: $\lambda_{max.}$ 284 mμ (log ε 3·36).

x-*Chloro*-y-*methyl*-2 : 3-*dimethoxydiphenyl*.—To methyl-lithium, from methyl iodide (2 g.) and lithium (0·2 g.), in ether (10 c.c.) stirred at 0° was added during 5 min. 5 : 6-dichloro-2 : 3-dimethoxydiphenyl [1] (1·42 g.) in ether (15 c.c.). The mixture was stirred at 0° for 1 hr., refluxed for 6 hr., and decomposed at 0° with water (20 c.c.), and the ethereal phase was separated, washed with water, and dried. Removal of the solvent and distillation of the residue gave an oil (1·1 g.), b. p. 109—110°/0·04 mm., which solidified and, on crystallisation from methanol, afforded the *diphenyl* as rhombic plates, m. p. 92·5° (Found: C, 68·6; H, 5·6; Cl, 13·4. $C_{15}H_{15}O_2Cl$ requires C, 68·6; H, 5·7; Cl, 13·5%). Light absorption: $\lambda_{max.}$ 288 mμ (log ε 3·36).

2 : 3-*Dihydroxy*-5 : 6-*dimethyldiphenyl*.—A mixture of 2 : 3-dimethoxy-5 : 6-dimethyldiphenyl (0·48 g.), powdered anhydrous aluminium chloride (1 g.), and dry chlorobenzene (10 c.c.) was refluxed for 3 hr., cooled, and added to 15% hydrochloric acid (40 c.c.). After being stirred vigorously for 30 min., the mixture was extracted with ether, the extract was washed with water and dried, and the solvent was removed. Trituration of the residue with a little cold light petroleum (b. p. 40—60°) and sublimation of the insoluble material at 145°/0·02 mm. gave a colourless solid (0·36 g., 85%) from which, by crystallisation from light petroleum (b. p. 80—100°), the *dihydroxydiphenyl* was obtained as needles, m. p. 171·5—172·5° (Found: C, 78·4; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). Light absorption: $\lambda_{max.}$ 291 mμ (log ε 3·46). Its *diacetate* formed rhombic plates, m. p. 111°, from aqueous ethanol (Found: C, 72·6; H, 6·0; Ac, 28·3. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·0; Ac, 28·9%).

5 : 6-*Dimethyl*-2 : 3-*diphenoquinone* (VI).—(*a*) Silver oxide,[12] from silver nitrate (0·25 g.), and anhydrous sodium sulphate (0·5 g.) were suspended in ether (6 c.c.), and 2 : 3-dihydroxy-5 : 6-dimethyldiphenyl (54 mg.) in ether (6 c.c.) was added. After being shaken at 20° for 20 min. the suspension was filtered and the red filtrate was cooled to −75°; the *quinone* (44 mg., 83%) separated as deep red plates with a golden reflex, m. p. 109—110° after sintering at 105° (Found: C, 78·9; H, 5·7. $C_{14}H_{12}O_2$ requires C, 79·3; H, 5·7%). Light absorption: $\lambda_{max.}$ 410 mμ (log ε 3·30).

(*b*) To a stirred solution of 2 : 3-dihydroxy-5 : 6-dimethyldiphenyl (54 mg.) in ethanol–water (5 c.c. each) at 20° was added all at once sodium iodate hydrate (110 mg.) in water–ethanol (5 c.c., 2·5 c.c.). After 1½ hr. the solid was collected, washed with 50% aqueous ethanol, then water, and dried *in vacuo*. The orange-brown product (15 mg.), m. p. 104—106° after sintering at 100°, was spectroscopically almost identical with the quinone prepared by method (*a*). Light absorption $\lambda_{max.}$ 410 mμ (log ε 3·28).

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University of Leeds. [*Received, May 22nd, 1956.*]

[11] Kleiderer and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 4219.
[12] Willstätter and Müller, *Ber.*, 1908, **41**, 2581.

## 744. *The Constitution of a Wheat-straw Hemicellulose.*

By G. O. Aspinall and Eric G. Meek.

A wheat-straw hemicellulose, containing uronic acid residues (*ca.* 3%), gave on hydrolysis xylose and arabinose in the ratio of 11 : 1. Hydrolysis of the methylated polysaccahride yielded 2 : 3 : 5-tri-*O*-methyl-L-arabinose, 2 : 3 : 4-tri-*O*-methyl-D-xylose, 2 : 3-di-*O*-methyl-D-xylose, 2-*O*-methyl-D-xylose, and 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid, together with some 3-*O*-methyl-2-*O*-(2 : 3 : 4-tri-*O*-methyl-D-glucuronosyl)-D-xylose. The structure of the polysaccharide is discussed in the light of these and other results.

Previous structural investigations have indicated that a variety of closely related polysaccharides constitute wheat-straw hemicellulose. Adams [1] and Bishop [2] showed that the hemicellulose contains a backbone of 1 : 4-linked β-D-xylopyranose residues, to which are attached through position 3 a number of L-arabofuranose and D-glucopyruronic acid residues as single-unit side-chains. Earlier studies in these laboratories [3] showed that it was possible to fractionate the hemicellulose and to isolate a xylan, devoid of arabinose residues, but still containing uronic acid residues as an integral part of the molecular structure. These investigations were carried out on hemicellulose fractions isolated by alkaline extraction from straw which had previously been treated with acidified sodium chlorite solution to remove lignin. In view of the possibility of degradation of polysaccharides during chlorite delignification,[4] we have now examined the hemicellulose extracted directly with alkali from wheat straw rather than from the holocellulose.

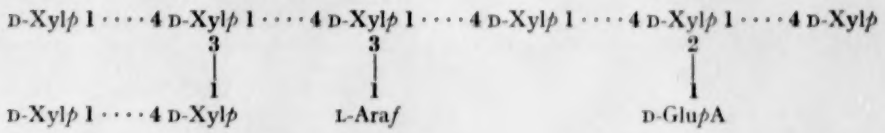
The hemicellulose was extracted from straw, previously extracted with benzene and methanol, by the procedure used in the extraction of beechwood hemicellulose A,[5] the structure of which we have previously studied.[6] The polysaccharide contained uronic acid residues (*ca.* 3%) and yielded on hydrolysis xylose and arabinose in the ratio of 11 : 1. Graded hydrolysis liberated arabinose preferentially, suggesting that this sugar occurred in the furanose form, but selective removal of these labile residues to yield a xylan devoid of arabinose residues could not be achieved without extensive degradation of the molecule, as appreciable quantities of xylose and xylose-containing oligosaccharides were released before all the arabinose residues had been removed. On more vigorous hydrolysis, a resistant acidic fraction was isolated; reduction of the derived methyl ester methyl glycoside with potassium borohydride, followed by hydrolysis, yielded 4-*O*-methylglucose, glucose, and xylose, indicating the presence in the polysaccharide of residues of glucuronic acid (partly as the 4-methyl ether).

The xylan was converted into its fully methylated derivative, hydrolysis of which yielded the following methylated sugars, characterised by the formation of crystalline derivatives: 2 : 3 : 5-tri-*O*-methyl-L-arabinose, 2 : 3 : 4-tri-*O*-methyl-D-xylose, 2 : 3-di-*O*-methyl-D-xylose, and 2-*O*-methyl-D-xylose (in the approximate ratio of 3 : 1 : 41 : 4). Small quantities of 3-*O*-methyl-D-xylose were also present; these probably arose from hydrolysis of some of the methylated aldobiouronic acid. In addition, 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid was characterised and an acidic fraction, consisting mainly of a tetra-*O*-methylaldobiouronic acid, was isolated. Insufficient of the latter fraction was isolated for a complete identification, but the following chromatographic studies leave little doubt concerning the structure of the main component. Reduction of the derived methyl ester methyl glycoside with lithium aluminium hydride, followed by hydrolysis, gave 2 : 3 : 4-tri-*O*-methylglucose and 3-*O*-methylxylose (clearly distinguished from the 2-methyl isomer by paper ionophoresis). Further methylation of the reduced acidic fraction, followed by hydrolysis,

[1] Adams, *Canad. J. Chem.*, 1952, **30**, 698.
[2] Bishop, *ibid.*, 1953, **31**, 134.
[3] Aspinall and Mahomed, *J.*, 1954, 1731.
[4] Timell and Jahn, *Svensk Papperstidning*, 1951, **24**, 831.
[5] McDonald, *J.*, 1952, 3183.
[6] Aspinall, Hirst, and Mahomed, *J.*, 1954, 1734.

yielded 2 : 3 : 4 : 6-tetra-*O*-methylglucose and 3 : 4-di-*O*-methylxylose, together with smaller amounts of 2 : 3 : 4-tri- and a mono-*O*-methylxylose. It follows that the tetra-*O*-methylaldobiouronic acid was 3-*O*-methyl-2-*O*-(2 : 3 : 4-tri-*O*-methylglucuronosyl)xylose. It is probable that the acidic fraction contained traces of a methylated aldotriouronic acid in addition to the tetra-*O*-methylaldobiouronic acid.

Although no unique structure can be advanced for this xylan, the results are consistent with the general type of structure shown :




In agreement with other workers,[1,7,8] we are of the opinion that the L-arabinose residues are integral parts of the molecule, occurring exclusively as end-groups in the furanose form. It is probable that these residues occur as single-unit side-chains linked to the backbone of β-1 : 4-D-xylopyranose residues through position 3 of xylose; direct proof for this mode of attachment has been provided by Bishop,[9] who isolated the trisaccharide, *O*-L-arabofuranosyl-(1→3)-*O*-D-xylopyranosyl-(1→4)-D-xylopyranose, from the enzymic hydrolysis of wheat-straw hemicellulose. The methylated aldobiouronic acid isolated from the hydrolysis of the methylated xylan shows that the D-glucuronic acid residues (partially present as the 4-methyl ether) are linked directly to the main chain through position 2 of xylose; previously, 1 : 3-linkages were reported for the aldobiouronic acid units in wheat-straw xylans.[2,3] Although the evidence for a 1 : 3-linked aldobiouronic acid unit in the arabinose-free xylan from wheat straw [3] rested solely on the chromatographic distinction between 2- and 3-*O*-methylxylose, it will be recalled that Bishop [2] provided conclusive proof for the structure of the aldobiouronic acid which he isolated from the hydrolysis of wheat straw. It seems probable, therefore, that the several wheat-straw xylans differ amongst themselves as to the mode of attachment of glucuronic acid to xylose residues, and, indeed, in some fractions [7] glucuronic acid residues appear to be absent. The 1 : 2-linked aldobiouronic acid unit found in this xylan is a common structural feature of wood hemicelluloses [6,10,11] and has also been encountered in oat-straw xylan.[12]

A molecular-weight determination by the isothermal-distillation method (by the courtesy of Dr. C. T. Greenwood and Mr. W. N. Broatch) gave a value of 11,800 ± 400 (degree of polymerisation, 71—76) for the methylated xylan. This value, taken together with the value of one non-reducing end-group per *ca.* 50 residues, suggests that some of the xylan chains are branched, probably through position 3. In this respect, this xylan differs from the arabinose-free xylan,[3] also isolated from wheat straw but after chlorite delignification, in which no evidence for branching was obtained. However, Bishop [13] has obtained evidence for branching in some wheat-straw hemicullulose fractions by the isolation of non-linear xylose-containing oligosaccharides on partial acid hydrolysis.

It is clear from these and previous results that many closely related polysaccharides may be derived from wheat straw; it is not certain, however, that all these different molecular species exist side by side in the same plant. Although it is possible that some of these may have arisen from the use of different methods of extraction, our earlier studies [3] have shown that xylans, differing significantly in the proportion of arabinose residues present, may be obtained by the fractionation of a particular wheat-straw hemicellulose. The present situation with regard to the detailed structure of wheat-straw xylan re-emphasises

[7] Ehrenthal, Montgomery, and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 5509.
[8] Roudier, *Compt. rend.*, 1953, **237**, 840; *Assoc. tech. ind. papetiere Bull.*, 1954, 53.
[9] Bishop, Amer. Chem. Soc. Meeting, Minneapolis, Sept., 1955, Abs. Papers 7E.
[10] Jones and Wise, *J.*, 1952, 3389.
[11] Gorrod and Jones, *J.*, 1954, 2522.
[12] Aspinall and Wilkie, *J.*, 1956, 1072.
[13] Bishop, *Canad. J. Chem.*, 1955, **33**, 1073.

the need for using the mildest possible methods for the extraction of polysaccharides from plant cell wall and for developing more selective methods for the fractionation of mixtures of polysaccharides.

## Experimental

Unless otherwise stated paper chromatography was carried out on Whatman No. 1 filter paper with the upper layers of the following solvent systems (v/v): (A) butan-1-ol–ethanol–water (4 : 1 : 5); (B) benzene–ethanol–water (167 : 47 : 15); (C) butan-1-ol–acetic acid–water (4 : 1 : 5); (D) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3); (E) pentan-1-ol–ethanol–water (2 : 1 : 2). Extractions and reactions involving the use of alkali were performed, as far as possible, under nitrogen.

*Isolation of Wheat-straw Xylan.*—Wheat straw, previously extracted with benzene and methanol, was ground in a "Raymond" laboratory mill, and the finely ground straw (150 g.; moisture content, 9·4%) was extracted successively with aqueous sodium hydroxide of increasing concentration (0·01N, 2 l. + 2 × 1·5 l.; 0·1N, 1·5 l.; N, 3 × 1·5 l.). The extracts with N-sodium hydroxide were acidified with glacial acetic acid to pH 4, and the precipitates (A) thus obtained were separated at the centrifuge. Further precipitates (B) were obtained on addition of an equal volume of ethanol to the supernatant liquors. A qualitative chromatographic examination of the sugars given on hydrolysis of the precipitates A and B indicated that the same sugars were present, so the polysaccharides were combined. The polysaccharide (37·3 g.) was purified by three precipitations from alkaline solution by the addition of acetic acid and ethanol. The purified polysaccharide had $[\alpha]_D^{19}$ −91·7° (*c*, 0·5 in N-sodium hydroxide) [Found: lignin, 7·2%; ash, 0·87%; uronic anhydride, 2·95% (by decarboxylation); OMe, 1·5%]. Chromatographic examination of the hydrolysate by Hirst and Jones's [14] method indicated the presence of xylose (90·6%) and arabinose (8·4%).

*Acid Hydrolysis of Xylan.*—(a) *Graded hydrolysis.* A suspension of xylan in 0·02N-oxalic acid was heated at 100°; samples were withdrawn at intervals, an equal volume of ethanol was added, and the precipitate was removed at the centrifuge. The precipitate was hydrolysed with 2N-sulphuric acid, and the hydrolysate was examined on the chromatogram with solvent A. The supernatant liquid was neutralised with barium carbonate and examined directly on the chromatogram. The results indicated that arabinose was rapidly released but that before all the arabinose residues were removed from the remaining polysaccharide (2 hr.) appreciable quantities of xylose and xylose-containing oligosaccharides could be detected in the supernatant liquid.

(b) *Examination of the acidic components in the hydrolysate.* Xylan (2·3 g.) was treated with 2N-sulphuric acid (50 ml.) at room temperature for 22 hr. and then heated at 100° for 4·5 hr.; the insoluble residue which remained was treated with 2N-sulphuric acid (50 ml.) at 100° for a further 5 hr. The combined hydrolysates were neutralised with barium carbonate, and the filtrate was de-ionised by treatment with Amberlite resin IR-120(H) and concentrated to a syrup (2·0 g.), which contained xylose, arabinose, glucose (trace), and acidic oligosaccharides. The syrup was fractionated on acid-washed charcoal–celite (1 : 1, w/w) (42 × 1·8 cm.), elution with water yielding monosaccharides together with a small quantity of acidic material (fraction 1), and elution with ethyl methyl ketone–water (5 : 95, v/v) yielding acidic oligosaccharides together with a trace of xylose (fraction 2). The acidic components from fraction 1 were separated on filter sheets with solvent D and combined with fraction 2. The acids were converted into the methyl ester methyl glycosides, reduced with potassium borohydride, and hydrolysed, chromatography showing 4-*O*-methylglucose, glucose, and xylose.

*Methylation of Xylan.*—Xylan (20·5 g.) was methylated fifteen times with methyl sulphate and sodium hydroxide. The fraction (5·1 g.) soluble in boiling chloroform–light petroleum (b. p. 60—70°) (9 : 11, v/v) but insoluble in boiling chloroform–light petroleum (1 : 4, v/v) was further methylated with methyl iodide and silver oxide to give a brown glass (4·77 g.) (Found: OMe, 36·0%). This material was fractionally precipitated from chloroform solution by the addition of light petroleum (b. p. 60—70°), and the fraction precipitated in light petroleum–chloroform (4 : 1) but not by light petroleum–chloroform (3 : 1 v/v) was used in subsequent experiments (Found: OMe, 38·3%).

*Hydrolysis of Methylated Xylan and Separation of Methylated Sugars.*—Methylated xylan (3·54 g.) was hydrolysed successively with boiling methanolic 1% hydrogen chloride (400 ml.)

[14] Hirst and Jones, *J.*, 1949, 1649.

for 6 hr. ($[\alpha]_D$ +58·7°, constant) and 0·5N-hydrochloric acid (200 ml.) for 7·5 hr. ($[\alpha]_D$ +18·6°, constant). After neutralisation with silver carbonate, the hydrolysate was taken to dryness to yield a syrup (3·75 g.). Quantitative paper chromatography [15] in solvent A showed the presence of tri-*O*-methylpentose (tri-*O*-methylarabinose and tri-*O*-methylxylose) (10·8%), di-*O*-methylxylose (75·5%), and mono-*O*-methylxylose (10·8%), together with small quantities of acidic substances. Quantitative chromatography in solvent B showed that tri-*O*-methylarabinose and tri-*O*-methylxylose were present in the ratio of 3 : 1. The syrup (3·5 g.) was fractionated on cellulose [16] (93 × 2·7 cm.) by elution with solvent B to yield seven fractions, and two further fractions were obtained by elution with butan-1-ol 50% saturated with water, and with water.

*Fraction* 1. The syrup (1 mg.) travelled on the chromatogram in solvent B at the same rate as 2 : 3 : 5-tri-*O*-methyl-L-arabinose and was combined with fraction 2*a*.

*Fraction* 2. Chromatographic examination of the syrup (282 mg.) in solvent B showed the presence of two components, which were separated on filter sheets (Whatman 3MM) with solvent B, to give fractions 2*a* and 2*b*. Fraction 2*a* had $n_D^{15}$ 1·4516 and was identified as 2 : 3 : 5-tri-*O*-methyl-L-arabinose by conversion into 2 : 3 : 5-tri-*O*-methyl-L-arabonamide, m. p. 134°. Fraction 2*b* crystallised and had m. p. and mixed m. p. (with 2 : 3 : 4-tri-*O*-methyl-D-xylose) 91—92° and $[\alpha]_D^{16}$ +18·2° (equil.) (*c*, 0·55 in $H_2O$). The derived 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-D-xylosylamine did not crystallise, but chromatographic examination of the syrup in butan-1-ol–pyridine–water (10 : 3 : 3) showed two components (corresponding to the glycosylamine and the parent sugar [17]) having the same rates of movement as those derived from an authentic sample.

*Fraction* 3. The syrup (4 mg.) travelled on the chromatogram in solvent B at the same rate as 2 : 3 : 4-tri-*O*-methyl-D-xylose and was combined with fraction 2*b*.

*Fraction* 4. The syrup (2·8 g.), when seeded with 2 : 3-di-*O*-methyl-α-D-xylose, crystallised as the β-anomer (full details have been published previously [18]). The identity of the sugar was confirmed by conversion into the aniline derivative, m. p. and mixed m. p. 123°, and into 2 : 3-di-*O*-methyl-D-xylonamide, m. p. and mixed m. p. 134°.

*Fractions* 5 *and* 7. Chromatographic examination of the syrup (105 mg.) indicated the presence of a major component having $R_{rhamnose}$ 1·64—1·78 in solvent C and giving a dipolar spot similar to that given by the acidic component isolated from the hydrolysis of methylated pear cell wall xylan,[19] together with small quantities of di-*O*-methylxylose. Reduction of the derived methyl glycoside methyl ester with lithium aluminium hydride, followed by hydrolysis, yielded sugars identified chromatographically as mono- and di-*O*-methylxylose and 2 : 3 : 4-tri-*O*-methylglucose.

*Fraction* 6. Chromatographic examination of the syrup (22 mg.) gave the same dipolar spot, with characteristic orange fluorescence in ultraviolet light, as that given by fractions 5 and 7. On hydrolysis with 2N-sulphuric acid at 100° for 44 hr., the slower-moving component decreased in amount, whilst the faster-moving component, which travelled at the same rate as 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid, increased, and mono-*O*-methylxylose was liberated. Complete hydrolysis was achieved by 2N-sulphuric acid at 100° in a sealed tube in 66 hr.; the products were separated on filter sheets with solvent C. The first component was identified as 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid by conversion into the β-methyl glycoside, m. p. 130—132°. Ionophoretic examination of the mono-*O*-methylxylose showed it to be mainly the 3-methyl ether with small quantities of the 2-methyl ether.

*Fraction* 8. The fraction (227 mg.) partially crystallised. The crystalline portion was ionophoretically homogeneous and had m. p. and mixed m. p. (with 2-*O*-methyl-D-xylose) 131—132° and $[\alpha]_D^{15}$ +28·9° (equil.) (*c*, 2·4 in $H_2O$). The identity of the sugar was confirmed by conversion into 2-*O*-methyl-*N*-phenyl-D-xylosylamine, m. p. and mixed m. p. 128—129°. The syrupy portion was shown ionophoretically to consist mainly of the 2-methyl ether with small amounts of the 3-methyl ether.

*Fraction* 9. The syrup (118 mg.) was chromatographically similar to fractions 5—7, but also contained traces of slow-moving components. Chromatography on filter sheets in solvent C yielded a purified acidic fraction, having $[\alpha]_D^{16}$ +10·2° (*c*, 0·1 in $H_2O$). The derived methyl ester methyl glycoside was reduced with lithium aluminium hydride, and the product was divided into two portions. The first portion was hydrolysed with 0·5N-hydrochloric acid at 100° for 8 hr., and quantitative chromatography [15] showed 2 : 3 : 4-tri-*O*-methylglucose and

[15] Hirst, Hough, and Jones, *J.*, 1949, 928.
[16] Hough, Jones, and Wadman, *J.*, 1949, 2511.
[17] Barclay, Foster, and Overend, *J.*, 1955, 1541.
[18] Meek, *J.*, 1956, 219.
[19] Chanda, Hirst, and Jones, *J.*, 1951, 1240.

mono-*O*-methylxylose to be present in the ratio of 1 : 1. The second portion was methylated twice with silver oxide and methyl iodide, and chromatography of the hydrolysate in solvents B and E showed 2 : 3 : 4 : 6-tetra-*O*-methylglucose, 2 : 3 : 4-tri-*O*-methylxylose, 3 : 4-di-*O*-methylxylose, and mono-*O*-methylxylose.

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DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, May 28th,* 1956.]

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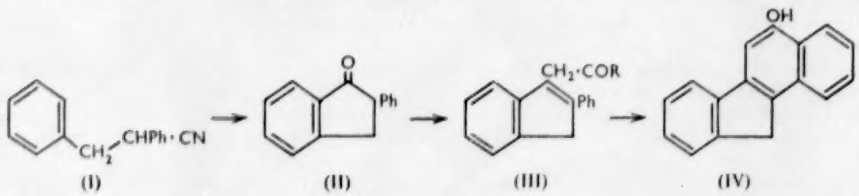
## 745. *A New Synthesis of* 3-*Hydroxy*-1 : 2-*benzofluorene.*

By NEIL CAMPBELL and ENGELBERT CIGANEK.

Convenient methods for the preparation of 2-phenylindanone and 3-hydroxy-1 : 2-benzofluorene are described.

THE preparation of 2-phenylindanone from αβ-diphenylproprionic acid [1] and deoxybenzoin [2] has been described. We find it may advantageously be obtained by condensing benzyl chloride with the sodium derivative of benzyl cyanide to give αγ-diphenylpropionitrile (I). Hydrolysis of this to the acid, followed by ring-closure, gives 2-phenylindanone (II) in an over-all yield of 30%.

3-Hydroxy(or 3-acetoxy)-1 : 2-benzofluorene has been prepared by reduction of the fluorenone.[3] It can also be readily prepared by treating 2-phenylindanone with ethyl bromoacetate and zinc, to give the ester (III; R = OEt) which after hydrolysis and conversion into the acid chloride is cyclised to 3-hydroxy-1 : 2-benzofluorene (IV). The



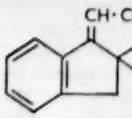

(I) (II) (III) (IV)

structure of the product was thus established, for not only does ring-closure occur preferentially to give a six-membered ring, but also ring-closure on the aromatic nucleus of the indanone ring would give a sterically improbable product with two five-membered rings annealed to one another and to the benzene ring.[4] The structure was confirmed by identity with that of the reduction product of 3-hydroxy-1 : 2-benzofluorenone [5] kindly supplied by Dr. J. D. Loudon.

The dehydration of the Reformatsky product may yield either the ester (III) or the isomer with an *exo*-double bond. Although elimination reactions of 5-membered rings favour the formation of an *exo*- rather than an *endo*-double bond [6] we favour formula (III) since the substance forms a colourless ureide with carbobis-*p*-dimethylaminophenylimide.[7] This is in harmony with Linstead's finding that at equilibrium *cyclo*pentenylacetic acid

[1] Von Auwers and Auffenberg, *Ber.*, 1919, **52**, 108.
[2] Plattner, Sandrin, and Wyss, *Helv. Chim. Acta*, 1946, **29**, 1604.
[3] Cook and Preston, *J.*, 1944, 553; Badger, Campbell, and Cook, *J.*, 1949, 1084; Gross and Lankelma, *J. Amer. Chem. Soc.*, 1951, **73**, 3439.
[4] See, *e.g.*, Cook and Hunter, *J.*, 1952, 3168.
[5] Jarrett and Loudon, *J.*, 1955, 4052.
[6] Brown, Brewster, and Shechter, *J. Amer. Chem. Soc.*, 1954, **76**, 467.
[7] Zetsche, *Ber.*, 1939, **72**, 1599.

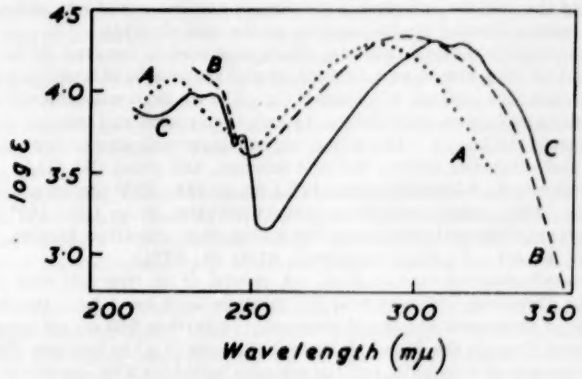
contains 96% of the βγ-isomer.[8] Our structure (III) was confirmed by the general similarity of the absorption spectrum of the acid to those of 2-phenylindene [9] and *trans*-stilbene [10] (see Figure). The preferential formation of an *endo*-double bond may be attributed in part to the conjugation of this bond with two phenyl nuclei. It is perhaps cogent that in the equilibrium $Ph{\cdot}CH_2{\cdot}CPh{:}CH{\cdot}CO_2H \rightleftharpoons Ph{\cdot}CH{:}CPh{\cdot}CH_2{\cdot}CO_2H$ the second acid with its phenyl nuclei conjugated through the ethylenic linkage occurs to the extent of 83%.[11]



(V)

2-Methyl-2-phenylindanylideneacetic acid (V) was prepared for comparison of its spectrum with that of our acid (III; R = OH), but it was not obtained in sufficient quantity to ensure that it was spectroscopically pure. With Zetsche's reagent in ether it gave a yellow solution.

*Absorption spectra of (A) 2-phenylindenylacetic acid, (B) trans-stilbene, and (C) 2-phenylindene.*




## Experimental

M. p.s were determined on the Kofler block.

*2-Phenylindanone.*—Freshly distilled benzyl cyanide (170 g.) was added during 1 hr. to powdered sodium (33 g.) and dry ether (600 ml.) under nitrogen. The mixture was boiled and stirred until all the sodium dissolved (*ca.* 2 hr.), then cooled to room temperature, and to it was added, during 30 min. with vigorous stirring, freshly distilled benzyl chloride (85 g.). The solution was stirred overnight, the ether boiled off, and dry benzene (600 ml.) added. The mixture was boiled for 2 hr., then cooled, and dilute hydrochloric acid added. The benzene layer was washed with aqueous sodium carbonate, water, and saturated aqueous sodium chloride, and dried ($Na_2SO_4$). Removal of the solvent and distillation yielded αβ-diphenylpropionitrile (63%), b. p. 138—145°/0·4—0·5 mm.

The nitrile (88 g.) was boiled for 10 hr. with trimethylene glycol (250 ml.), sodium hydroxide (35 g.), and water (80 ml.) and poured into water. Unchanged nitrile was removed in benzene; and the alkaline solution with hydrochloric acid gave αβ-diphenylpropionic acid (88%), m. p. 95° after two crystallisations from light petroleum (b. p. 60—80°). The acid (50 g.) was converted by phosphorus pentachloride into the acid chloride, which was added in benzene dropwise to a stirred cooled suspension of aluminium chloride (38 g.) in dry benzene (500 ml.; "AnalaR"). The mixture was stirred for 3 hr. at room temperature, ether (100 ml.) was added, and the complex decomposed by aqueous hydrochloric acid (1 : 1). The organic layer was washed with sodium carbonate solution, water, and saturated sodium chloride solution, and dried ($Na_2SO_4$). Removal of the solvent and distillation gave 2-phenylindanone (67%), b. p. 145—155°/0·4—0·5 mm., m. p. 78° after crystallisation from light petroleum (b. p. 60—80°).

[8] Linstead, *J.*, 1928, 2343; 1930, 1603.
[9] Wiegand and Merkel, *Annalen*, 1942, **550**, 175.
[10] Arends, *Ber.*, 1931, **64**, 1936.
[11] Phalnikar and Nargund, *J. Univ. Bombay*, 1939, **8**, III, 184.

3-*Hydroxy*-1 : 2-*benzofluorene*.—2-Phenylindanone (23 g.), benzene (50 ml.), ethyl bromoacetate (25 g.), and iodine (trace) were added to amalgamated zinc wool (20 g.) in dry benzene (150 ml.) and dry ether (150 ml.). The mixture was heated to start the reaction and when this was complete heating was resumed (4 hr.), more bromo-ester (2 × 10 g.) and amalgamated zinc (5 × 4 g.) being added at intervals. The colourless addition product was decomposed by a little ethanol and acetic acid, the solution poured into acetic acid and water (1 : 1), and the organic layer separated, washed with water, and dilute ammonia, and dried ($Na_2SO_4$). The solvent was removed and the residue dehydrated by a crystal of iodine at 200°/100 mm. during 30 min. Distillation yielded ethyl 2-phenylindenylacetate, b. p. 168—178°/0·6 mm., which was hydrolysed when boiled for 2 hr. with potassium hydroxide (7 g.), ethanol (50 ml.), and water (50 ml.) to pale-yellow 2-*phenylindenylacetic acid* (21·2 g., crude), m. p. 144° [after crystallisation from benzene–light petroleum (b. p. 60—80°)] (Found : C, 81·4; H, 5·6. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%). The acid in ether with a slight excess of carbobis-*p*-dimethylaminophenylimide deposited overnight the colourless *ureide*, m. p. 245° after sintering at 198° (Found : C, 76·4; H, 6·5; N, 10·8. $C_{34}H_{34}O_2N_4$ requires C, 76·9; H, 6·5; N, 10·6%).

Ring-closure of the acid by polyphosphoric acid or sulphuric acid was unsuccessful, but was achieved by the inverse Friedel–Crafts reaction on the acid chloride. The acid (1 g.) and phosphorus pentachloride gave the acid chloride, which, dissolved in benzene (50 ml.; " AnalaR "), was added during ½ hr. dropwise to an ice-cooled, stirred suspension of finely powdered aluminium chloride (0·7 g.) in benzene (500 ml.; " AnalaR "). The ice-bath was removed and the mixture stirred until the temperature reached 20° (*ca.* 1½ hr.), then cooled and treated with ether (50 ml.) and hydrochloric acid (1 : 1 v/v). The yellow organic layer was washed with sodium carbonate solution, water, and saturated sodium chloride solution, and dried ($Na_2SO_4$). Removal of the solvent gave 3-hydroxy-1 : 2-benzofluorene (42%), m. p. 215—223° (decomp.) depending on the rate of heating (lit., 219°), which yielded an acetyl derivative, m. p. 159—160° (lit., 155—156°), and with dimethyl sulphate and alkali gave the *methyl ether*, colourless needles, m. p. 142—143° (Found : C, 87·2; H, 5·7. $C_{16}H_{14}O$ requires C, 87·8; H, 5·7%).

2-*Methyl*-2-*phenylindanylideneacetic Acid*.—A crystal of an iron salt was added to sodium (0·37 g.) in liquid ammonia (100 ml.) and the mixture kept for 1 hr. Dry benzene (50 ml.) was added dropwise to remove the liquid ammonia; a further 150 ml. of benzene were added and nitrogen passed through the flask. 2-Phenylindanone (3 g.) in benzene (20 ml.) was added to the stirred suspension of sodamide, and the mixture boiled for 3 hr., cooled to 40°, and treated dropwise with methyl iodide (10 g.) in benzene (20 ml.). The mixture was again boiled for 3 hr., then cooled and decomposed by dilute hydrochloric acid. The organic layer was washed with aqueous sodium hydrogen sulphite and sodium carbonate, then with water, and dried ($Na_2SO_4$). Removal of the solvent gave 2-*methyl*-2-*phenylindanone* (44%), m. p. 110—111° after crystallisation from light petroleum (b. p. 60—80°) (Found : C, 86·5; H, 6·4. $C_{16}H_{14}O$ requires C, 86·5; H, 6·4%).

This indanone (1 g.) in benzene (20 ml.) and dry ether (20 ml.) was treated with ethyl bromoacetate (2·5 g.) and amalgamated zinc (2 g.) as described above. The product was dehydrated by iodine at 210°/100 mm. The resulting oil in benzene was washed with aqueous sodium hydrogen sulphite, aqueous sodium carbonate, and water, and dried, and the solution evaporated. The residue was hydrolysed for 1 hr. with potassium hydroxide (0·5 g.) in boiling water (10 ml.) and ethanol (10 ml.). Acidification afforded 2-*methyl*-2-*phenylindanylideneacetic acid* (34%), m. p. 175—176° (rapid heating) after crystallisation from benzene–light petroleum (b. p. 60—80°) (Found : C, 82·2; H, 6·2. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

*Spectroscopic Measurements*.—The ultraviolet spectra were measured by means of a Unicam SP.500 Spectrophotometer with *cyclo*hexane as solvent. 2-Phenylindenylacetic acid, $\lambda_{max.}$ 227 and 288 mμ (log ε 4·03 and 4·27 respectively), and $\lambda_{min.}$ 248 mμ (log ε 3·63). 2-Phenylindene, $\lambda_{max.}$ 230, 237, 246, 306, and 314 mμ (log ε 4·08, 4·08, 3·84, 4·28, and 4·28 respectively).

We thank the British Petroleum Co. Ltd. for a grant, Dr. D. H. Reid for a sample of 2-phenylindene, and Mr. A. G. Cairns-Smith and Mr. D. A. Crombie for assistance in the practical work.

Department of Chemistry, University of Edinburgh. [*Received, June 4th,* 1956.]

## 746. *Magnetic Studies with Copper(II) Salts. Part I. Anomalous Paramagnetism and δ-Bonding in Anhydrous and Hydrated Copper(II) Acetates.*

By B. N. Figgis and R. L. Martin.

The temperature variation of the magnetic susceptibilities of anhydrous and hydrated copper(II) acetates has been determined between 90° and 400° K. The results establish well-defined maxima in the susceptibility curves at 270° and 255° K from which an exchange interaction between adjacent copper atoms in each of the binuclear molecules may be calculated to be 302 and 286 cm.$^{-1}$ respectively. These values indicate the existence of very weak covalent copper–copper bonds in which the exchange contribution to the total bond energy is approx. 1 kcal. mole$^{-1}$.

The nature of the bond is discussed from the valency-bond point of view and it is suggested that a δ-bond is formed between adjacent copper atoms by lateral overlap of $3d_{x^2-y^2}$ orbitals, the $z$-axis being taken as along the line joining the copper atoms. Copper acetate, according to this hypothesis, is the first case in which a δ-bond is the sole direct link between two atoms.

The diamagnetism reported for the isostructural chromous acetate is consistent with the presence of weak σ-, π-, and δ-bonds between each pair of chromium atoms.

The experimental susceptibilities for the copper acetates agree with those calculated theoretically from an expression similar to one first developed by Bleaney and Bowers.[1] Some discrepancies below 200° K in two earlier determinations of the susceptibility of hydrated copper acetate are discussed.

The magnetic behaviour of crystalline cupric acetate monohydrate $Cu(CH_3{\cdot}CO_2)_2{,}H_2O$ has excited considerable interest since Lifschitz and Rosenbohm [2] in 1915, using the Curie method, found that the molar susceptibility $\chi_M$ at room temperature was much less than the value, $10^6 \times \chi_M \sim 1600$, usually observed for copper salts. With the exception of some measurements by Bhatnagar, Singh, and Ghani [3] in 1932, all subsequent investigations [4,5,6,7,8] have confirmed that the susceptibility of copper acetate at room temperature is anomalously low.

The first study of the temperature variation of the susceptibility of a single crystal of the hydrate (between 83° and 304° K) was made in 1951 by Guha.[6] Instead of obeying some form of the expected Curie–Weiss law, the susceptibility was found to pass through a probable maximum near 270° K and to fall rapidly below this temperature, the extrapolated value being zero at 20° K. The main features of Guha's curve were confirmed by Foex, Karantassis, and Perakis [7] for the powdered hydrate between 87° and 288° K. However, below *ca.* 200° K considerable discrepancies exist between the results from these two schools, so that re-investigation seemed necessary before an attempt to correlate experiment and theory quantitatively. In addition, the higher temperature used did not establish the maximum unequivocally or enable the form of the susceptibility curve at, say, 150° above the maximum to be assessed. Further, extrapolation of Guha's results leads to $\chi_M = 0$ at *ca.* 20° K whereas Foex *et al.* report 75° K.

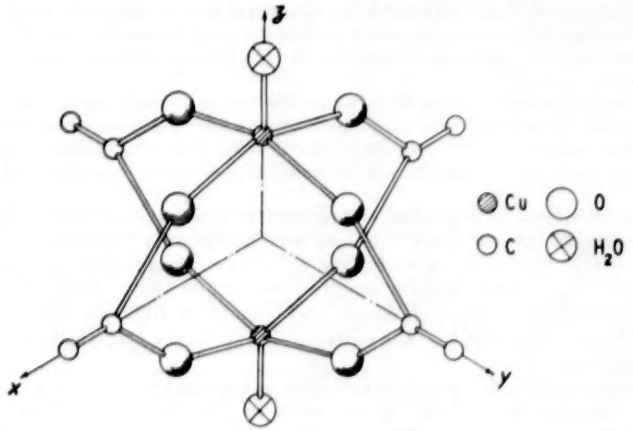
Evidence that this anomalous magnetic behaviour arises from some form of strong coupling between the unpaired electrons on adjacent copper atoms through exchange forces was obtained from the anomalous behaviour of both powdered [9] and single crystal

[1] Bleaney and Bowers, *Proc. Roy. Soc.*, 1952, *A*, **214**, 451.
[2] Lifschitz and Rosenbohm, *Z. Electrochem.*, 1915, **21**, 499.
[3] Bhatnagar, Singh, and Ghani, *Indian J. Phys.*, 1932, **7**, 323.
[4] Amiel, *Compt. rend.*, 1938, **207**, 1097.
[5] Mookerjee, *Indian J. Phys.*, 1945, **19**, 63.
[6] Guha, *Proc. Roy. Soc.*, 1951, *A*, **206**, 353.
[7] Foex, Karantassis, and Perakis, *Compt. rend.*, 1953, **237**, 982.
[8] Gauthier, *ibid.*, 1954, **238**, 1999.
[9] Lancaster and Gordy, *J. Chem. Phys.*, 1951, **19**, 1181.

specimens [1,10,11,12] of copper acetate towards paramagnetic resonance absorption of microwaves in the range 9—50 kMc./sec. ($\lambda = 0{\cdot}6$—$3{\cdot}3$ cm.). In particular, Bleaney and Bowers [1] explained convincingly both the susceptibility curves obtained by Guha and the paramagnetic absorption data by suggesting that isolated pairs of copper atoms interact strongly through exchange forces, each pair forming a lower singlet state and an upper triplet state, only the latter being paramagnetic. As the temperature is lowered the singlet level becomes increasingly populated at the expense of the triplet level so that the susceptibility decreases steadily, eventually to zero. In the absence of either crystallographic data or isomorphous diamagnetic dilution data (as suggested by Mookerjee [9]) they were unable to decide whether direct spin interaction occurred between adjacent copper atoms or whether the interaction forces were of Kramer's super-exchange type,[13,14] acting through intermediate oxygen atoms.

The latter problem has been recently resolved by Niekerk and Schoening's complete structure determination [15] which shows that copper acetate monohydrate is a binuclear molecule $Cu_2(CH_3{\cdot}CO_2)_4{,}2H_2O$ in which copper atoms are bridged in pairs by four acetate groups with two water molecules occupying the terminal positions (cf. Fig. 1).

FIG. 1. *Structure of the cupric acetate monohydrate molecule.*




A remarkable feature of the structure is the close distance of approach of the two copper atoms (2·64 Å) which is only slightly greater than the interatomic distance in metallic copper (2·56 Å). Clearly, the postulated exchange interaction between electron spins is of a direct nature rather than of the super-exchange type, and may be described as the overlap of atomic orbitals of the two copper atoms.

The present work was undertaken as part of a programme of cryomagnetic investigations on polycrystalline inorganic compounds in which exchange interactions of an antiferromagnetic nature play an important role.[16] The specific objects were: First, as mentioned above, a re-investigation of the temperature dependence of the susceptibility of $Cu(CH_3{\cdot}CO_2)_2{,}H_2O$, to resolve discrepancies in and to extend earlier measurements. Secondly, to evaluate directly the magnitude of the exchange energy, $J$, in preference to the procedure employed by Bleaney and Bowers in which they chose an empirical value for $J$ which gave the best fit to Guha's susceptibility data (the latter now seem to be up to 100% in error at the lower temperatures). Thirdly, to examine in detail the nature of

[10] Bleaney and Bowers, *Phil. Mag.*, 1952, **43**, 372.
[11] Kumagai, Abe, and Shimada, *Phys. Rev.*, 1952, **87**, 385.
[12] Abe and Shimada, *ibid.*, 1953, **90**, 316.
[13] Anderson, *ibid.*, 1950, **79**, 350.
[14] Lidiard, *Reports Progr. Phys.*, 1954, **17**, 201.
[15] Nierkerk and Schoening, *Acta Cryst.*, 1953, **6**, 227.
[16] Martin, Nyholm, and Stephenson, *Chem. and Ind.*, 1956, 83.

the bonding orbitals used by each copper atom, and to extend the examination to the isostructural diamagnetic chromous acetate. In addition, the temperature variation of the susceptibility of anhydrous copper acetate was studied to determine whether the magnitude of the exchange interaction was altered by the concomitant modification of the crystalline field acting on each copper atom.

## Experimental

*Materials.*—Large single crystals of cupric acetate monohydrate were obtained by recrystallization of "AnalaR" copper acetate from dilute acetic acid. They were transparent green or blue diamond-shaped plates. Grinding the crystals with an agate pestle and mortar gave an opaque blue-green powder which was used in the magnetic measurements: its water content was determined by the Fischer method and by dehydration over phosphoric oxide *in vacuo* at 118°. The anhydrous acetate is similar in colour to the hydrated form. Copper was determined by electrolytic deposition on a platinum electrode, the carbon and hydrogen contents by the conventional micro-methods (Anhydrous copper acetate—Found: Cu, 34·9; C, 26·4; H, 3·27. Calc. for $CuC_4H_6O_4$: Cu, 35·0; C, 26·4; H, 3·33%. Hydrated copper acetate—Found: Cu, 31·7; C, 24·4; H, 4·18; $H_2O$, 9·0. Calc. for $CuC_4H_6O_4.H_2O$: Cu, 31·8; C, 24·1; H, 4·04; $H_2O$, 9·0%).

*Magnetic Measurements.*—The magnetic susceptibilities of the anhydrous and the hydrated powdered specimens were determined by the Gouy method, in nitrogen between 90° and 400° K, an apparatus developed by Figgis and Nyholm [17] being used. The specimen was maintained at within ±0·05° for 1—2 hr. at each temperature before measurement. The field strength employed was about 8000 gauss, ±0·1%. The chief source of error arose from the packing of the powder in the Gouy tube and, for this reason, the absolute accuracy of the determinations was no better than ±1%, even though the self-consistency of the measurements was much better.

*Results.*—The values obtained are contained in Tables 1 and 2. The molar susceptibility

Table 1. *Experimental gram and molar susceptibilities and magnetic moments of* $Cu(CH_3{\cdot}CO_2)_2$.

| Temp. (K) | 93·0° | 105·5° | 126·0° | 153·2° | 182·8° | 211·5° |
|---|---|---|---|---|---|---|
| $10^6 \times \chi_g$ (c.g.s., e.m.u.) | 0·890 | 1·30 | 2·04 | 2·96 | 3·71 | 4·18 |
| $10^6 \times \chi_M$ (c.g.s., e.m.u.) | 234 | 309 | 442 | 609 | 745 | 831 |
| $\mu$ (B.M.) | 0·361 | 0·460 | 0·623 | 0·824 | 1·01 | 1·15 |
| Temp. (K) | 240·5° | 268·5° | 295·4° | 332·6° | 398·9° | |
| $10^6 \times \chi_g$ (c.g.s., e.m.u.) | 4·36 | 4·43 | 4·39 | 4·33 | 4·05 | |
| $10^6 \times \chi_M$ (c.g.s., e.m.u.) | 865 | 877 | 869 | 858 | 808 | |
| $\mu$ (B.M.) | 1·25 | 1·33 | 1·39 | 1·46 | 1·55 | |

Table 2. *Experimental gram and molar susceptibilities and magnetic moments of* $Cu(CH_3{\cdot}CO_2)_2.H_2O$.

| Temp. (K) | 93·5° | 100·1° | 120·2° | 143·5° | 160·5° | 181·0° | 200·9° | 220·0° |
|---|---|---|---|---|---|---|---|---|
| $10^6 \times \chi_g$ (c.g.s., e.m.u.) | 0·907 | 1·09 | 1·83 | 2·64 | 3·14 | 3·52 | 3·77 | 3·95 |
| $10^6 \times \chi_M$ (c.g.s., e.m.u.) | 266 | 302 | 451 | 612 | 712 | 787 | 837 | 873 |
| $\mu$ (B.M.) | 0·39 | 0·44 | 0·62 | 0·80 | 0·92 | 1·03 | 1·12 | 1·20 |
| Temp. (K) | 239·7° | 258·6° | 277·9° | 294·2° | 300·3° | 321·3° | 349·5° | 396·5° |
| $10^6 \times \chi_g$ (c.g.s., e.m.u.) | 4·05 | 4·07 | 4·06 | 4·03 | 4·02 | 3·96 | 3·85 | 3·57 |
| $10^6 \times \chi_M$ (c.g.s., e.m.u.) | 893 | 858 | 895 | 889 | 878 | 876 | 854 | 797 |
| $\mu$ (B.M.) | 1·27 | 1·32 | 1·37 | 1·40 | 1·42 | 1·45 | 1·50 | 1·54 |

$\chi_M$ (per mole of copper ions) includes a diamagnetic correction of $-72 \times 10^{-6}$ (cf. Mookerjee [8]) for $Cu(CH_3{\cdot}CO_2)_2$, and $-85 \times 10^{-6}$ for the hydrated salt. The effective magnetic moment $\mu$ has been calculated at each temperature from the expression $\mu = 2{\cdot}839[(\chi_M - N\alpha)T]^{0.5}$, where $N\alpha$ represents the temperature-independent paramagnetism associated with the copper ion. In the present work, a value $N\alpha = 60 \times 10^{-6}$ has been used (cf. refs. 1 and 18).

[17] Figgis and Nyholm, unpublished work.
[18] Polder, *Physica*, 1942, **9**, 709.

The present room-temperature susceptibilities are compared in Table 3 with earlier values. The agreement is good except with that by Bhatnagar, Singh, and Ghani [3] now thought to be erroneous.

The variation with temperature, of the molar susceptibility and the magnetic moment, is shown in Figs. 2 and 3. The susceptibility curve of hydrated copper acetate exhibits a broad

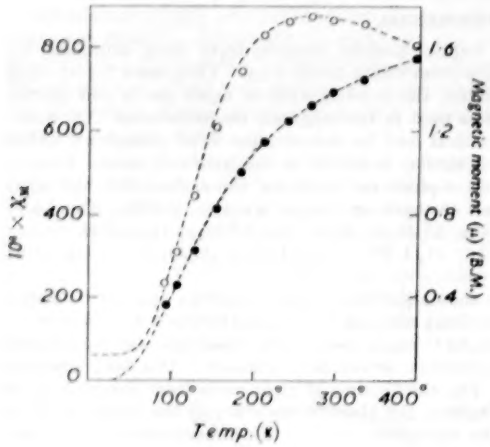
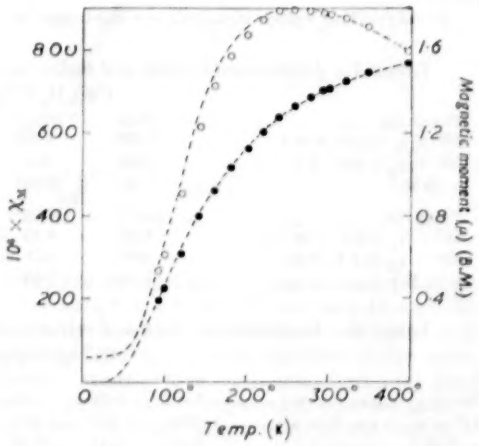



FIG. 2. *Experimental and calculated magnetic susceptibilities and moments of anhydrous cupric acetate.*

○ *Experimental susceptibility,* $10^6 \times \chi_M$.
● *Experimental moment,* $\mu$.
– – – – *Calc. from eqn.* 4.

FIG. 3. *Experimental and calculated magnetic susceptibilities and moments of cupric acetate monohydrate.*

○ *Experimental susceptibility,* $10^6 \times \chi_M$
● *Experimental moment,* $\mu$.
– – – – *Calc. from eqn.* 5.




maximum in the region of 250° K, whereas the corresponding temperature for the anhydrous compound is some 20° higher. The exact positions of the maxima were established from graphical plots of $\delta\chi/\delta T$ against the temperature $T$, the intercept on the axis $\delta\chi/\delta T = 0$ being taken as the critical temperature $T_c$. In this way, values of 270° and 255° K were obtained for the anhydrous and hydrated compounds. Above the critical temperature $T_c$, the susceptibility

TABLE 3. *Comparison of room-temperature molar susceptibilities* ($10^6 \times \chi_M$, c.g.s., e.m.u.; temp. in parentheses).

$Cu(CH_3 \cdot CO_2)_2$ : 869 (22·2°) *; 885 (20°).[4]
$Cu(CH_3 \cdot CO_2)_2 \cdot H_2O$ : 889 (21·0°) *; 1024 (18°) [2]; 1585 (?) [2]; 890 (20°) [4]; 852 (30°) [5]; 858 (31·2°) [6]; 879 (14·6°) [7]; 905 (16°).[8]

* Present work.

fell gradually but Curie–Weiss law behaviour had not been established at 400° K. Below $T_c$ the susceptibility fell rapidly, so that at 90° K it was only one-quarter of the maximum value. For both compounds, the magnetic moment ($\mu$) rises steadily from ~0·4 at 90° K to ~1·6 at 400° K. The spin-only value $\mu = 1{\cdot}73$ would be attained at *ca.* 500° K, but, unfortunately, thermal decomposition at these temperatures would vitiate direct measurement.

The present values for $Cu(CH_3{\cdot}CO_2)_2,H_2O$ agree well (see Fig. 4) with those obtained by

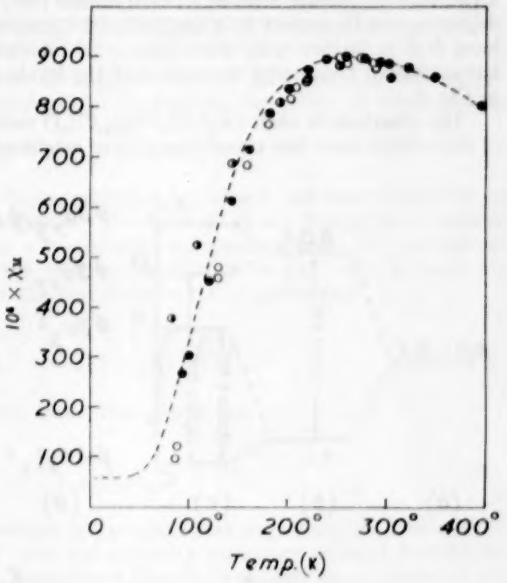



FIG. 4. *Comparison of magnetic susceptibilities of cupric acetate monohydrate.*

● *Present work.*
○ Foex *et al.*
◑ Guha.
– – – *Calc. from eqn. 5.*

Guha and by Foex *et al.* at 200—300° K, but below 200° K Guha's results are too high, suggesting the presence of a paramagnetic impurity in his material, and at their lowest recorded temperature (87° K) Foex *et al.* give $10^6 \times \chi_M = 98$ compared with the present value of 230.

## Discussion

Bleaney and Bowers [1] first accounted for the anomalous susceptibility of hydrated copper acetate (using Guha's results) in terms of two hypotheses : (*a*) " that isolated pairs of copper ions interact strongly through exchange forces, each pair forming a lower singlet and an upper triplet state, only the latter being paramagnetic " and (*b*) " that the crystalline field acting on each copper ion is similar to that in other salts such as Tutton's salts." The latter hypothesis has recently been shown to be substantially correct by the *X*-ray evidence of Niekerk and Schoening.[15] However, in order adequately to fit Guha's data to their theoretical expression an empirical value for the exchange integral was necessary, *viz.*, $J = 315$ cm.$^{-1}$, whereas their paramagnetic resonance experiments had led to $J = 259 \pm 26$ cm.$^{-1}$. It will be shown below that the exchange integral can be related directly to the critical temperature $T_c$, so that it may be determined directly from the magnetic data.

The spectroscopic ground state of a free $Cu^{++}$ ion is $^2D_{5/2}$ corresponding to a fully occupied 3*d* shell minus one electron. The *D*-state is five-fold degenerate in the free ion if electron spin is neglected. Bethe [19] has shown that under the influence of a cubic crystalline field (as occurs when the $Cu^{++}$ ion is at the centre of a perfect octahedron of oxygen atoms) this degeneracy is partly removed and the multiplet is split into two levels, one two-fold degenerate *A*, *C* and the other three-fold degenerate *B*, *D*, *E* with an energy difference of

[19] Bethe, *Ann. Physik*, 1929, **3**, 133.

about 13,000 cm.$^{-1}$. In the present case, there is a departure from cubic symmetry owing to some distortion of the octahedral co-ordination of each $Cu^{++}$ along the $z$-axis (cf. Fig. 1), but to a first approximation the symmetry may be regarded as equivalent to that obtained by imposing a component of tetragonal symmetry on the cubic field. In a field of this symmetry with the $z$-axis as symmetry axis, the level $A$, $C$ is split up into two non-degenerate levels $A$ and $C$, whereas the level $B$, $D$, $E$ is split into a non-degenerate level $D$ and a two-fold degenerate level $B$, $E$, each orbital level having, of course, an additional double degeneracy with respect to a magnetic field associated with the electron spin of $\frac{1}{2}$. The level $B$,$E$ is further split when spin–orbit interaction is taken into account. Polder [18] has estimated the energy separation of the levels under these conditions to be as shown in Fig. 5.

The situation in each $Cu_2(CH_3{\cdot}CO_2)_4{,}2H_2O$ molecule is modified owing to the overlap of the orbital wave functions belonging to neighbouring copper ions which are only 2·64 Å

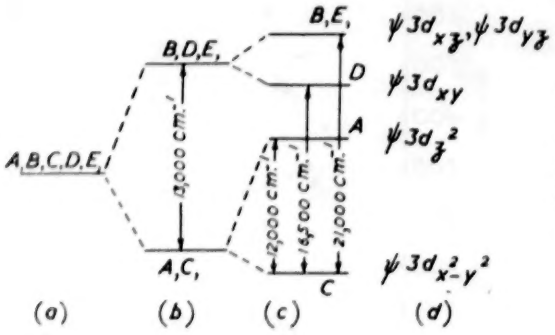
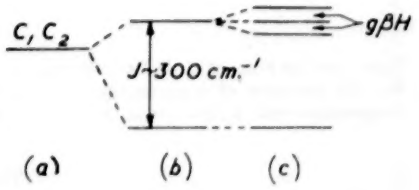



FIG. 5. *Energy level diagram for the $d^9$ configuration of $Cu^{2+}$.*
*(a) $^2D$ state of the free ion.*
*(b) splitting of the orbital levels in an electric field of cubic symmetry.*
*(c) further splitting due to tetragonal component of the field.*
*(d) wave functions for each orbital level.*

FIG. 6.
*(a) Lowest energy level of a system of two interacting $Cu^{++}$–$Cu^{++}$ ions under the influence of a cubic and tetragonal field.*
*(b) Splitting into a singlet and a triplet due to the exchange interaction.*
*(c) Further splitting of the triplet in a magnetic field.*




apart. Following the argument development by Bleaney and Bowers, the number of orbital levels now becomes $5 \times 5 = 25$, each with a degeneracy in spin of $2 \times 2 = 4$. The lowest of these "molecular" states may be denoted by $C_1C_2$ since its wave function is the product of the individual wave functions $C$ for the ions $Cu_1^{++}$ and $Cu_2^{++}$. The four-fold spin degeneracy is partly removed by the exchange interaction which splits the level into a singlet and a triplet with an energy separation equal to $J$. The singlet is diamagnetic with $S = 0$ and is the ground state, whereas the triplet level is paramagnetic and behaves like a state of spin $S = 1$. Under the influence of an applied magnetic field $H$, the degeneracy in the triplet is lifted, the level splitting into three levels of energy separation equal to $g\beta H$ where $g$ is the spectroscopic splitting factor and $\beta$ is the Bohr magneton. The splitting of the molecular $C_1C_2$ level by the exchange interaction is shown diagrammatically in Fig. 6.*

The magnetic properties of hydrated copper acetate will be primarily determined by the energy-level diagram illustrated in Fig. 6. In a general way, it will be seen that, as the temperature is raised above the absolute zero, the paramagnetic triplet level becomes

* The effect of spin–orbit coupling, and the zero field splitting of the triplet level into a singlet and a doubtlet, which it is not essential to mention here, are discussed in the paper by Bleaney and Bowers.[1]

populated at the expense of the diamagnetic singlet level so that the susceptibility rapidly increases until a maximum value is reached at $T_c$. Above this temperature the usual decrease in susceptibility with rise in temperature is observed.

An expression for the molar susceptibility can be readily obtained from Van Vleck's basic formula :[20]

$$\chi_M = \frac{N\sum_{nm}\left\{\frac{E_{nm}^{(1)2}}{kT} - 2E_{nm}^{(2)}\right\}\exp\left(-E_n^{(0)}/kT\right)}{\sum_n g_n \exp\left(-E_n^{(0)}/kT\right)} \quad . \quad . \quad . \quad . \quad (1)$$

where $E_n^{(0)}$ denotes energy levels under no applied magnetic field and $E_{nm}^{(1)}$ and $E_{nm}^{(2)}$ denote coefficients of the first- and second-order Zeeman displacements of levels defined by the relation,

$$E_{nm} = E_n^{(0)} + E_{nm}^{(1)}H + E_{nm}^{(2)}H^2$$

The magentic field removes the spin degeneracy of $g_n$ of level $n$ and these sublevels are specified by the magnetic quantum number $m$. Terms in $H^2$ do not change the separation of the four orbital levels but introduce a temperature-independent term $N\alpha$ into the susceptibility which is not affected by the relative distribution of $Cu^{++}$ ions between the singlet and the triplet state. Thus, to the first order of the magnetic field,

$$\chi_M = \frac{2g^2N\beta^2}{3kT} \cdot \frac{1}{1 + \frac{1}{3}\exp\left(J/kT\right)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

If the magnetic moment arises from spin alone, then $g = 2$ and

$$\chi_M = \frac{0{\cdot}500}{T} \cdot \frac{1}{1 + \frac{1}{3}\exp\left(J/kT\right)} + N\alpha \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$N\alpha$ is included to represent the temperature-independent paramagnetism per mole of $Cu^{++}$ ions. It follows that $\chi_M = N\alpha$ when $T = 0$, and rises to a maximum value at $T_c \simeq 5J/8k$, so that the exchange energy can be determined directly from the temperature of the maximum, $J = 1{\cdot}6kT_c$. The Curie–Weiss law will not be strictly obeyed until $T \gg T_c$ when $\theta \simeq 0{\cdot}4T_c$.[14]

*Comparison of Experimental and Theoretical Data.*—Susceptibility maxima in anhydrous and hydrated copper acetates were observed at 270° and 255° K, leading to the values 432° K (= 302 cm.$^{-1}$) and 408° K (= 286 cm.$^{-1}$) for the respective exchange interactions. The latter figure is in fair agreement with Bleaney and Bowers's estimate of $J = 259 \pm 26$ cm.$^{-1}$ from paramagnetic resonance experiments. If it is assumed that $N\alpha = 60 \times 10^{-6}$ and that $J$ is effectively independent of temperature, the splitting factor $g$ can be calculated by substituting the experimental values of the maximum susceptibility at $T_c$ into equation (2). In this way, values $g = 2{\cdot}17$ and $2{\cdot}13$ are obtained for the anhydrous and the hydrated compounds respectively. The latter figure may be compared with those obtained by Bleaney and Bowers, $g = 2{\cdot}19$, and Abe and Shimada,[12] $g = 2{\cdot}16$, from paramagnetic resonance experiments. The resulting susceptibility equations are :

$$Cu(CH_3{\cdot}CO_2)_2 : \ 10^6 \times \chi_M = \frac{0{\cdot}586}{T} \cdot \frac{1}{1 + \frac{1}{3}\exp\left(432/T\right)} + 60 \quad . \quad . \quad (4)$$

$$Cu(CH_3{\cdot}CO_2)_2,H_2O : \ 10^6 \times \chi_M = \frac{0{\cdot}568}{T} \cdot \frac{1}{1 + \frac{1}{3}\exp\left(408/T\right)} + 60 \quad . \quad . \quad (5)$$

The experimental results are compared in Figs. 2 and 3 with those calculated from these equations. The agreement is remarkably good, even though the values below $T_c$ tend to

[20] Van Vleck, "The Theory of Electric and Magnetic Susceptibilities," Oxford Univ. Press, 1932, p. 182.

lie slightly below the calculated curves. Contrary to Bleaney and Bowers's view this indicates that anisotropic thermal expansion along the *z*-axis produced by an increase in temperature decreases the overlap of 3*d* wave functions on neighbouring $Cu^{++}$ ions, and the exchange interaction would accordingly be lowered. This is in harmony with the calculations of the overlap integral $S(3d_{x^2-y^2}-3d_{x^2-y^2})$ by Craig *et al.*[21] which show, for example, that a 10% increase in the Cu–Cu distance of 2·64 Å would halve the overlap integral.

The deviation of the *g*-values from the free-spin value, $g = 2$, indicates that spin–orbit coupling cannot here be neglected, and that an orbital contribution to the magnetic moment arises from mixing of some of the upper " molecular " states of the binuclear molecule into the ground $C_1C_2$ level.

The small increase in $J$ of 16 cm.$^{-1}$ observed on dehydration of copper acetate may well be a real effect, even though small. The *X*-ray data have indicated a small displacement (0·22 Å) of each Cu atom out of its $CuO_4$ plane, indicating a repulsion between neighbouring Cu atoms, probably due to overlap of their filled $3d_{z^2}$, $3d_{zz}$, and $3d_{yz}$ orbitals. However, on removal of the terminal water molecules, overlap along the *z*-axis will be decreased, and the concomitant decrease in the Cu–Cu distance will result in an increased $3d_{x^2-y^2}$–$3d_{x^2-y^2}$ exchange interaction.

*The Nature of the* Cu–Cu *Bond in Copper Acetate.*—The bonding orbitals in each binuclear $Cu_2(CH_3{\cdot}CO_2)_4{,}2H_2O$ unit are best described in valency-bond rather than molecular-orbital language since the overlap integral $S(3d_{x^2-y^2}-3d_{x^2-y^2})$ is small. In each molecule, two square pyramidal $CuO_5$ groups are held together, base to base, by four bridging acetate groups, the fifth oxygen atom belonging to a terminal water molecule (cf. Fig. 1). The bonding orbitals used by each copper atom are best described as four square planar $4s4p^24d$ hybrid orbitals, together with a fifth 4*p* orbital lying along the *z*-axis at right angles to the $CuO_4$ plane. This agrees better with the observed Cu–O distances (Cu–O in the planar $CuO_4$ group = 1·97 Å whereas Cu–$H_2O$ = 2·20 Å) than an alternative description involving *s*-character in all five bonds. The use of " upper " *d*-orbitals in copper(II) compounds is well recognized where the ligands are highly electronegative, as in the present compound (cf. Craig *et al.*[21]).

Of particular interest in the present work is the nature of the bond between the neighbouring copper atoms in each binuclear molecule. The bond type (*i.e.*, $\sigma$, $\pi$, $\delta$, etc.) will be determined by the particular 3*d*-orbital occupied by an unpaired electron in the ground state, whereas the bond energy will be determined, in part, by the magnitude of the overlap of these 3*d*-orbitals. If the electron configuration $3d^9$ is considered as a fully filled 3*d* level containing one " positive hole," it follows that the ground state will correspond to the " positive hole " occupying that 3*d* orbital which has its lobes in the direction of the negative, and hence electron-repelling, ligands. This corresponds to the $3d_{x^2-y^2}$ orbital, a conclusion which has been verified theoretically by the work of Polder (cf. Fig. 5). Polder has estimated that the $3d_{z^2}$ orbital level in the $[Cu(H_2O)_6]^{++}$ ion lies 12,000 cm.$^{-1}$ above the $3d_{x^2-y^2}$ level owing to an elongation of the $CuO_6$ octahedron along the *z*-axis. Further destabilization of the $3d_{z^2}$ orbital arises, in the present compound, from replacement of a highly electronegative oxygen ligand by a weakly electronegative copper atom on the *z*-axis. It might be argued that if a Cu–Cu bond arising from " end-on " overlap of two $3d_{z^2}$ orbitals along the *z* axis were sufficiently stronger than one resulting from lateral overlap of two $3d_{x^2-y^2}$ orbitals, then the former would become the favoured bond type, in spite of the separation of 12,000 cm.$^{-1}$ referred to above. However, an evaluation of the overlap integral, $S(3d_{z^2}-3d_{z^2}) = 0{\cdot}046$ (see next section), does not support this possibility, but indicates that such a bond, while certainly stronger than that arising from $3d_{x^2-y^2}$–$3d_{x^2-y^2}$ overlap, is quite unlikely to be sufficiently strong to be preferred on energy grounds. It is therefore concluded that the observed exchange interaction between unpaired spins on adjacent copper atoms arises from lateral overlap of $3d_{x^2-y^2}$ orbitals oriented with their lobar planes parallel. The link between neighbouring copper atoms may be described as a $\delta$-bond : it is illustrated in Fig. 7.

Calculation of the overlap integral, *S*, using the expression quoted by Craig *et al.*,

[21] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 332.

gives a value consistent with the above conclusion that $3d_\delta$–$3d_\delta$ overlap is involved. Thus a value $S(3d_\delta\text{–}3d_\delta) = 0{\cdot}003$ is obtained by using the values $t = 0$ and $p = 12$, where $t$ and $p$ are independent variables giving a measure of nuclear asymmetry and internuclear distance respectively of the bond. This value may be compared, for example, with the $\pi$-overlap in a homonuclear bond such as C=C where $S(2p_\pi\text{–}2p_\pi) \sim 0{\cdot}2$—$0{\cdot}3$, indicating that the present exchange energy is very much smaller. The exchange energies determined from the magnetic data (286 and 302 cm.$^{-1}$) are equivalent to an energy contribution of slightly less than 1 kcal. mole$^{-1}$. Although the weakly electronegative copper ligands will favour the formation of a $\delta$-bond between themselves, it must of necessity be very weak because of the dependence of the wave function $\psi_{3d_{x^2-y^2}}$ on $\sin^2\theta$ which concentrates the orbital function in the $xy$ plane. This minimizes the overlap with a parallel function except at internuclear distances much smaller than 2·64 Å.

Copper acetate, according to the above hypothesis, is the first case in which a $\delta$-bond

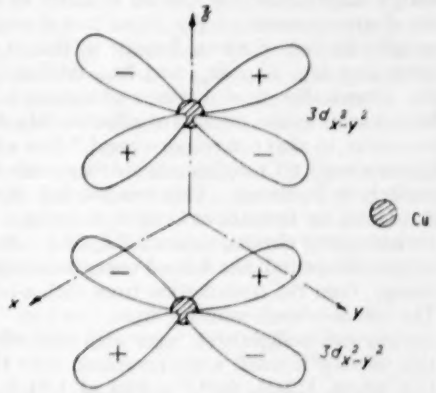



FIG. 7. *δ-Bonding arising from lateral overlap of two $3d_{x^2-y^2}$ orbitals oriented with their lobar planes parallel.*

is the sole direct link between two atoms. However, the bond is so weak that the configuration of the binuclear molecule can only be maintained by the four bridging acetate groups. Reference to the bond as a " metallic " copper–copper bond (cf. refs. 22 and 23) seems to us inappropriate, and the more accurate description as " a very weak covalent δ-bond " between two copper atoms is preferable.

This type of bonding is not confined to copper acetate alone, and experimental evidence will be presented in Part II of this series which indicates that probably all copper(II) salts of straight-chain fatty acids are binuclear molecules of general formula $Cu_2(C_nH_{2n+1}\cdot CO_2)_4,xH_2O$ where $x$ is generally 0 or 2. The behaviour of single crystals of copper propionate to paramagnetic resonance absorption of microwaves strongly resembles that of the acetate, and has led to the proposal that strong exchange interactions are also present in this compound.[24] Polarized absorption spectra in the visible and the near-ultraviolet region have recently been reported for both copper acetate and copper propionate, and the presence of a new absorption band at $80 \times 10^{13}$ c./sec. (3750 Å) has been taken as a further indication of a direct linkage between two copper atoms in these compounds.[25] The apparently anomalous variation of magnetic susceptibility with temperature of copper laurate reported [26] in 1953 can now also be safely ascribed to a further example of δ-bonding between two copper atoms in a fatty acid salt.

*Diamagnetism of Chromous Acetate.*—The magnetic behaviour of chromous acetate is of interest in the present connection. King and Garner [27] have shown that both anhydrous

[23] Niekerk and Schoening, *Nature*, 1953, **171**, 36.
[24] Speakman, *Ann. Rep.*, 1954, **51**, 390.
[25] Abe, *Phys. Rev.*, 1953, **92**, 1572.
[26] Tsuchida and Yamada, *Nature*, 1955, **176**, 1171.
[27] Gilmour and Pink, *J.*, 1953, 2198.
[27] King and Garner, *J. Chem. Phys.*, 1950, **18**, 689.

and hydrated chromous acetate are diamagnetic, and, in the absence of *X*-ray data, interpreted this result as the first example of tetrahedral $3d^5 4s$-bond hybridization. However, a recent *X*-ray structure determination [22,28] invalidated their conclusion and showed that chromous acetate is also a binuclear molecule $Cr_2(CH_3{\cdot}CO_2)_4{,}2H_2O$ isostructural with copper acetate.

In its simple and complex salts with highly electronegative ligands chromium(II) normally exhibits a magnetic moment corresponding to the presence of four unpaired electrons,[29] so that the observed diamagnetism is, at first sight, surprising. However, it is explained if both the directional properties of the chromium 3*d*-orbitals and the short Cr–Cr internuclear distance are taken into account. If, as in the case of the copper analogue, four $4s4p^24d$ chromium orbitals are used for bonding each planar $CrO_4$ group and the remaining $4p$ orbital is used for bonding a terminal water molecule, then four unpaired electrons occupy $3d$ levels in each chromium atom. Orgel [30] has pointed out that the energy diagram for the quintet *D* states of the $d^4$-configuration is identical with that of the $d^9$-arrangement (cf. Fig. 5), so that it seems probable that the ground state will correspond with zero electron density in the $3d_{x^2-y^2}$ orbital, the remaining four $3d$ electrons occupying $3d_{z^2}$, $3d_{xz}$, $3d_{yz}$, and $3d_{xy}$ orbitals in accordance with Hund's rule. Owing to the abnormally close distance of approach between chromium atoms (2·64 Å) in each binuclear molecule, overlap of adjacent $3d_{z^2}$–$3d_{z^2}$, $3d_{xz}$–$3d_{xz}$, $3d_{xz}$–$3d_{yz}$, and $3d_{xy}$–$3d_{xy}$ orbitals can occur, so that one *schedo*-σ-bond,*, two π-bonds, and one δ-bond are formed. Since the internuclear Cr–Cr distance is identical with that observed in copper acetate the bonds are unlikely to be strong. This conclusion is supported by evaluation of the overlap integrals *S*. Using the formulæ of Craig *et al.* with $t = 0$ and $p = 12$ as the appropriate independent variables, one obtains values $S(3d_\pi\text{–}3d_\pi) = 0{\cdot}021$ and $S(3d_\delta\text{–}3d_\delta) = 0{\cdot}003$. If, as with the copper compound, the δ-bond contributes approximately 1 kcal. mole$^{-1}$ to the Cr–Cr bond energy, then the contribution from each π-bond is probably of the order of 5 kcal. mole$^{-1}$. The *schedo*-σ-bond resulting from "end-on" overlap of two $3d_{z^2}$ orbitals along the internuclear axis is slightly stronger with $S(3d_{z^2}\text{–}3d_{z^2}) = 0{\cdot}046$ (see Appendix). However, even this overlap is small when compared with the σ overlap in a homonuclear bond such as C–C where $S(2sp^3_\sigma\text{–}2sp^3_\sigma) = 0{\cdot}64$ at 1·54 Å.[31] On this basis, the Cr–Cr bond must be regarded as weak, although it is probably considerably stronger than its Cu–Cu counterpart, the bonds in both cases being supported by the bridging acetate groups. The resulting exchange is apparently sufficient effectively to pair the spins of the eight electrons occupying $3d$ levels in each chromous acetate molecule and to account for the observed diamagnetism.

## Appendix

We are indebted to Mr. E. A. Magnusson for evaluating the overlap integral for the *schedo*-σ-type bond resulting from "end-on" overlap of two $3d_{z^2}$ orbitals along a common *z*-axis. This integral has not previously been evaluated, for this is probably the first compound in which this type of overlap appears to play a significant part in the bonding of two atoms.

The explicit expression for the overlap integral (using the nomenclature of Craig *et al.*) is:

$$S(3d_{z^2}\text{–}3d_{z^2}) = \frac{(1-t^2)^{7/2}p^7}{1152}\,[A_0(-9B_2 + 6B_4 - B_6) + A_2(9B_0 - 3B_4 + 6B_6) + A_4(-6B_0 + 3B_2 - 9B_6) + A_6(B_0 - 6B_2 + 9B_4)]$$

The authors thank Dr. E. Challen for carbon and hydrogen microanalyses, and Professor D. P. Craig for helpful discussion.

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* The nomenclature follows that suggested by Craig *et al.*

[28] Nieckerk, Schoening, and de Wet, *Acta Cryst.*, 1953, **6**, 501.
[29] Hume and Stone, *J. Amer. Chem. Soc.*, 1941, **63**, 1200.
[30] Orgel, *J. Chem. Phys.*, 1955, **23**, 1004.
[31] Mulliken, Reike, D. Orloff, and H. Orloff, *J. Chem. Phys.*, 1949, **17**, 1248.

## 747. *Purines, Pyrimidines, and Glyoxalines. Part III.* A New Synthesis of 2-Thiouracils.*

By M. R. Atkinson, G. Shaw, K. Schaffner, and R. N. Warrener.

5-Cyano-2-ethylthio-4-oxo-1 : 3-thiazine (V) results from the reaction of ethyl *N*-cyanoacetyldithiocarbamate (I), ethyl orthoformate, and acetic anhydride. Treatment of the thiazine with primary amines and subsequent treatment of the products with sodium hydroxide solution gave derivatives of 2-thiouracil.

2-Thiouracil and its derivatives have assumed some importance in recent years in the treatment of hyperthyroidism and as metabolite antagonists.[1] The literature records two general synthetical routes to the thiouracils, namely, the condensation of thiourea with a β-oxo-ester [2] or derivative, and the substitution of oxygen in a preformed oxygenated pyrimidine by sulphur.[3–5] Earlier papers in this series [6] have described a general synthesis of 5-cyanouracils by reaction of primary amines with α-cyano-β-ethoxy-*N*-ethoxycarbonylacrylamide, particularly convenient for the preparation of 1-substituted uracils. For tests of similar 2-thiouracils as potential antimetabolites, and for other reasons, this reaction has now been extended to derivatives of dithiocarbamic acid.

Cyanoacetic acid and ethyl dithiocarbamate in acetic anhydride at 25° give a readily separable mixture of ethyl *N*-cyanoacetyl- (I) and *N*-acetyl-dithiocarbamate (II), but at higher temperatures afford also the diacyl compound (III). An attempt to convert the cyanoacetyldithiocarbamate (I) into the ethoxymethylene derivative (IV) by reaction with ethyl orthoformate and acetic anhydride gave 5-cyano-2-ethylthio-4-oxo-1 : 3-thiazine (V) instead, by cyclisation.

$CN{\cdot}CH_2{\cdot}CO{\cdot}NH{\cdot}CS_2Et$ (I)

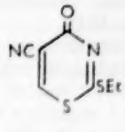
$Me{\cdot}CO{\cdot}NH{\cdot}CS_2Et$ (II)

$CN{\cdot}CH_2{\cdot}CO{\cdot}NAc{\cdot}CS_2Et$ (III)

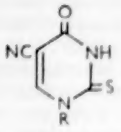
$CN{\cdot}C(:CH{\cdot}OEt){\cdot}CO{\cdot}NH{\cdot}CS_2Et$ (IV)

$CN{\cdot}C(:CH{\cdot}NHR){\cdot}CO{\cdot}NH{\cdot}CS_2Et$ (VI)

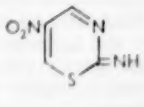
$CN{\cdot}CH_2{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}SEt$ (VIII)



(V)



(VII)



(IX)

The thiazine structure (V), assigned on the basis of analysis and chemical reactions, is confirmed by the infrared weak absorption band (Nujol mull) at 2250 cm.$^{-1}$ (CN) and the strong double band at 1650—1622 cm.$^{-1}$ (CO). A somewhat similar reaction, between thiourea and nitromalondialdehyde, has been reported to give the thiazine (IX).[7] The thiazine (V) reacted very readily at room temperature with ammonia, methylamine, and

* Part II, *J.*, 1956, 1877.

[1] Roblin, *Chem. Rev.*, 1946, **38**, 255; Wright, *Vitamins and Hormones*, 1951, **9**, 131; Woolley, "A Study of Antimetabolites," Wiley, New York, 1952; Albert, "Selective Toxicity with Special Reference to Chemotherapy," Methuen, London, 1951.

[2] Wheeler and Bristol, *Amer. Chem. J.*, 1905, **33**, 458; Wheeler and Liddle, *ibid.*, 1908, **40**, 550; de Bollemont, *Bull. Soc. chim. France*, 1901, **25**, 20; Anderson, Halverstadt, Miller, and Roblin, *J. Amer. Chem. Soc.*, 1945, **67**, 2197.

[3] Elion and Hitchings, *J. Amer. Chem. Soc.*, 1947, **69**, 2138; Russell, Elion, Falco, and Hitchings, *ibid.*, 1949, **71**, 2279; Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353.

[4] Wheeler and Liddle, ref. 2; Wheeler and McFarland, *Amer. Chem. J.*, 1910, **43**, 19.

[5] McOmie and Boarland, *Chem. and Ind.*, 1950, 602; *J.*, 1951, 1218; 1952, 3722.

[6] Parts I and II, *J.*, 1955, 1834; 1956, 1877.

[7] Hale and Brill, *J. Amer. Chem. Soc.*, 1912, **34**, 295.

aniline, to give the linear aminomethylene derivatives (VI; R = H, Me, and Ph) in excellent yields, the last two of which with aqueous sodium hydroxide gave the corresponding 2-thiouracils (VII; R = Me and Ph). Similarly, the thiazine and an alkaline solution of glycine gave directly the thiouracil (VII; R = $CH_2 \cdot CO_2H$). The linear compound (VI; R = H) was unexpectedly recovered unchanged from solutions in aqueous sodium hydroxide and ethanolic sodium ethoxide; it was eventually converted, in low yield, into 5-cyano-2-thiouracil (VII; R = H) when warmed for several hours with dilute sodium hydroxide solution. An increased yield of 5-cyano-2-thiouracil was obtained by the reaction of the thiazine with ammonia in acetonitrile, and in the presence of triethylamine.

In a parallel experiment, ethyl *N*-cyanoacetylthiocarbamate (VIII) was obtained in low yield from cyanoacetic acid and *O*-ethyl thiocarbamate at 80—100° in acetic anhydride. When it was heated with ethyl orthoformate and acetic anhydride, however, extensive decomposition occurred.

## Experimental

*Ethyl N-Cyanoacetyldithiocarbamate.*—Cyanoacetic acid (8·5 g.) and ethyl dithiocarbamate (12·1 g.) were shaken with acetic anhydride (11 ml.) at 25° for 60 hr. The resulting precipitate was filtered off, washed with a little ether (2 × 30 ml.), and extracted (Soxhlet) with ether (150 ml.) for 18 hr.; *ethyl N-cyanoacetyldithiocarbamate* (5·7 g.) crystallised from the extract as yellow needles, m. p. 140—142° and, recrystallised from methanol, had m. p. 142° (Found: C, 38·1; H, 4·1; N, 14·6. $C_6H_8ON_2S_2$ requires C, 38·3; H, 4·3; N, 14·9%). Evaporation of the original filtrate *in vacuo* gave ethyl *N*-acetyldithiocarbamate (5·7 g.) which separated from water as yellow needles, m. p. and mixed m. p. 124°.

*Ethyl N-Acetyl-N-cyanoacetyldithiocarbamate.*—A solution of cyanoacetic acid (51 g.) and ethyl dithiocarbamate (73 g.) in acetic anhydride (220 ml.) was kept at 80—100° for 0·5 hr. On cooling crystallisation occurred; the solid (42 g.) was filtered off, washed with ether (2 × 50 ml.), and recrystallised from methanol, to give a mixture of pale yellow and bright yellow needles. The latter were removed by washing with hot ether (5 × 10 ml.), to leave *ethyl N-acetyl-N-cyanoacetyldithiocarbamate* (3·3 g.) which separated from acetic acid as pale yellow needles; the m. p. was 194—196° (decomp.) when the compound was placed on a metal block at 180° and heated rapidly, otherwise the substance decomposed below 200° without melting (Found: C, 41·95; H, 4·6; N, 12·45. $C_8H_{10}O_2N_2S_2$ requires C, 41·7; H, 4·4; N, 12·2%). The residue obtained by evaporation of the ether and alcohol filtrates was crystallised from water, to give ethyl *N*-acetyldithiocarbamate (26 g.), m. p. and mixed m. p. 124°.

*5-Cyano-2-ethylthio-4-oxo-1 : 3-thiazine.*—Ethyl *N*-cyanoacetyldithiocarbamate (20 g.), ethyl orthoformate (28 g.), and acetic anhydride (40 ml.) were boiled under reflux for 1 hr. The red solution, when cooled, gave crystals which were filtered off and washed with a little ice-cold ethyl acetate; *5-cyano-2-ethylthio-4-oxo-1 : 3-thiazine* (8·5 g.) separated from benzene–carbon tetrachloride as orange-yellow leaflets, m. p. 140° (Found: C, 42·8; H, 2·9; N, 14·1. $C_7H_6ON_2S_2$ requires C, 42·4; H, 3·05; N, 14·1%). The filtrate was evaporated and the residue boiled under reflux for 1 hr.; when the solution was cooled a further quantity of the thiazine (4 g.) separated. The crude thiazine obtained in these experiments is pure enough for most purposes.

*5-Cyano-1-phenyl-2-thiouracil.*—To a solution of the thiazine (1 g.) in warm benzene (10 ml.) was added aniline (0·5 g.); the solution was cooled; after several minutes, crystals appeared (crystallisation may be induced with a seed crystal a few seconds after mixing); *ethyl N-(β-anilino-α-cyanoacryloyl)dithiocarbamate* (1·1 g.) separated from ethanol as yellow laths, m. p. 149° (decomp., resolidified, and then had m. p. 267°) (Found: C, 53·9; H, 4·4; N, 14·3. $C_{13}H_{13}ON_3S_2$ requires C, 53·6; H, 4·5; N, 14·45%). The anilino-compound (0·35 g.) rapidly dissolved when heated at 80° for 10 min. with aqueous 0·5N-sodium hydroxide (10 ml.), and ethanethiol was evolved. The solution was acidified with 2N-sulphuric acid (3 ml.), yielding pale yellow *5-cyano-1-phenyl-2-thiouracil* (0·24 g.) which crystallised from acetic acid as pale yellow plates, m. p. 267° (Found: C, 57·6; H, 3·3; N, 18·0. $C_{11}H_7ON_3S$ requires C, 57·65; H, 3·1; N, 18·3%).

*5-Cyano-1-methyl-2-thiouracil.*—To a solution of the thiazine (1 g.) in warm methanol (20 ml.) was added ethanolic methylamine (33%) until the smell of the base persisted. The solution was kept at room temperature for 5 min., then treated with an excess of N-sulphuric acid to precipitate cream-coloured *ethyl N-(α-cyano-β-methylaminoacryloyl)dithiocarbamate* (0·9 g.)

which separated from ethanol as pale yellow laths, m. p. 138° (Found: C, 42·05; H, 4·7; N, 18·3. $C_8H_{11}ON_3S_2$ requires C, 41·9; H, 4·85; N, 18·35%). This derivative (0·5 g.) was heated with N-sodium hydroxide (5 ml.) at 80—100° for 10 min., the solution cooled and acidified, and the precipitated *5-cyano-1-methyl-2-thiouracil* (0·27 g.) obtained from water as very pale yellow prisms, m. p. 295° (decomp.) (Found: C, 42·95; H, 2·85; N, 25·05. $C_6H_5ON_3S$ requires C, 43·1; H, 3·0; N, 25·15%).

*5-Cyano-2-thiouracil.*—(*a*) To a solution of the thiazine (1 g.) in benzene (50 ml.) was added ethereal ammonia until the smell of ammonia persisted; a small precipitate was obtained. The solution was evaporated to dryness *in vacuo* and the residue dissolved in N-sodium carbonate (20 ml.); the solution was acidified, to precipitate an oil which soon crystallised; *ethyl* N-(β-*amino-α-cyanoacryloyl*)*dithiocarbamate* (0·6 g.) separated from ethanol as yellow laths, m. p. 135° (Found: C, 39·0; H, 4·15; N, 19·3. $C_7H_9ON_3S_2$ requires C, 39·05; H, 4·2; N, 19·55%); it was recovered from an ethanolic solution containing sodium ethoxide after 24 hr. at room temperature. The amine (0·5 g.) was heated on a water-bath with 0·1N-sodium hydroxide (50 ml.) for 5 hr.; ethanethiol was evolved and a pale yellow solution was obtained; this was neutralised with hydrochloric acid and evaporated to dryness *in vacuo*; the residue, crystallised from water, gave 5-cyano-2-thiouracil (0·05 g.) as pale yellow prisms, m. p. 285° (decomp.) (Found: C, 38·9; H, 1·65; N, 27·4. Calc. for $C_5H_3ON_3S$: C, 39·2; H, 1·95; N, 27·45%); Anderson *et al.*[2] give m. p. 282—283° (decomp.).

(*b*) A solution of the thiazine (1·3 g.) in warm acetonitrile (12 ml.) was added to a mixture of 15N-ammonia (3 ml.) and triethylamine (1 ml.). The solution was heated at 60—80° for 10 min., treated with 15N-ammonia (3 ml.), and evaporated to dryness *in vacuo*. The residue was dissolved in water (20 ml.), and the solution adjusted to pH 12 with sodium hydroxide solution, then heated on a water-bath for 5 min., cooled, and brought to pH 4 with hydrochloric acid; 5-cyano-2-thiouracil (0·5 g.) separated and, recrystallised from water or butan-1-ol, had m. p. and mixed m. p. 283° (decomp.).

*1-Carboxymethyl-5-cyano-2-thiouracil.*—The preceding thiazine (1 g.) and glycine (0·4 g.) in 2N-sodium hydroxide (6 ml.) were heated at 80° for 10 min. Ethanethiol was liberated, and a clear pale yellow solution was obtained; this was cooled and acidified with 10N-hydrochloric acid (1·5 ml.); the precipitated *1-carboxymethyl-5-cyano-2-thiouracil* (0·65 g.) separated from water as orange-yellow plates, m. p. 340° (Found: C, 40·0; H, 2·8; N, 19·5. $C_7H_5O_3N_3S$ requires C, 39·8; H, 2·4; N, 19·9%).

*O-Ethyl N-Cyanoacetyl(thiocarbamate).*—Cyanoacetic acid (14·2 g.), *O*-ethyl thiocarbamate (16 g.), and acetic anhydride (20 ml.) were heated together at 85° for 0·5 hr.; much decomposition and darkening occurred but the cooled solution gave a crystalline precipitate; *O-ethyl N-cyanoacetyl(thiocarbamate)* (2·5 g.) separated from methanol as colourless needles, m. p. 198° (Found: C, 41·6; H, 4·8; N, 16·3. $C_6H_8O_2N_2S$ requires C, 41·85; H, 4·7; N, 16·3%). An attempt to obtain this compound by keeping the reactants at 25° for several days was unsuccessful.

We thank the N.S.W. State Cancer Council for a research grant and Dr. E. Challen and Mr. D. Weedon for the microanalyses.

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## 748. *Solutions in Sulphuric Acid. Part XX.* Cryoscopic Measurements on Some Aromatic Sulphides, Sulphoxides, and Sulphones.*

By R. J. Gillespie and R. C. Passerini.

Cryoscopic measurements have been made on solutions of a number of aromatic sulphides, sulphoxides, and sulphones in sulphuric acid. The results show that all the compounds studied behave as bases in sulphuric acid. The sulphides and sulphoxides are strong bases, but the sulphones are rather weak bases and are only partially ionised. Diphenyl sulphone and various substituted diphenyl sulphones are stable in sulphuric acid, but diphenyl sulphide and diphenyl sulphoxide undergo sulphonation and oxidation. Both the sulphides and sulphoxides are deactivated towards sulphonation and oxidation by the introduction of $NO_2$ and $NH_3^+$ substituents. The effect of nitro-substituents on the basicities of the sulphide and sulphone group is discussed. Some of our results and conclusions differ from those obtained by Szmant and Brost.[1]

It was first shown by Gillespie [2] that diphenyl sulphone behaves as a weak base in sulphuric acid. A wider investigation of the behaviour of a variety of aromatic sulphides, sulphoxides, and sulphones when dissolved in 100% sulphuric acid has since been carried out by Szmant and Brost, and Szmant and Lapinski,[1] who came to some unexpected conclusions; *e.g.*, they claimed that their results showed that diphenyl sulphoxide ionises according to the equation

$$Ph_2SO + 3H_2SO_4 = Ph_2S^{++} + H_3O^+ + 3HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

forming the diphenylsulphidonium ion $Ph_2S^{++}$. They also reached the surprising conclusion that the introduction of *p*-nitro-groups into diphenyl sulphone increases the basicity of the sulphone group.

It seemed desirable, therefore, to obtain some more information on the behaviour of this group of compounds. We have accordingly made a careful cryoscopic investigation of a number of aromatic sulphides, sulphoxides, and sulphones, some of which had been previously studied by Szmant and Brost. As some of the van't Hoff *i*-factors on which their conclusions were based appeared to be considerably in error, it was necessary to repeat their work. They did not, as is necessary for basic solutes, use as a solvent sulphuric acid in which the self-ionisation had been adequately repressed by the addition, for example, of a sufficient quantity of water; nor did they alternatively make any allowance in their calculations for the incompleteness in the repression of the self-ionisation equilibria. That is why their *i*-factors must be in error, and since, in general, the total freezing-point depressions from which they were calculated were rather small (0·2—0·5°) the errors may be considerable, probably as much as 100% in some cases.

### Experimental

*Apparatus and Procedure.*—The apparatus and general procedure for making the cryoscopic measurements have already been described.[3] When the change in the freezing point over a period of time was measured, the cryoscope was maintained at 20° ± 1° between measurements.

*Materials.*—The method of preparation of the sulphuric acid solvent has been described.[4] The organic solutes were prepared as described below. They were all purified by crystallisation to constant m. p., followed by at least five further crystallisations.

4 : 4′-Dinitrodiphenyl sulphide was prepared by refluxing an ethanol solution of 1-chloro-4-nitrobenzene with a freshly prepared concentrated aqueous solution of sodium sulphide;[5] recrystallised from acetic acid, it had m. p. 158°.

4-Aminodiphenyl sulphide was prepared by reducing 4-nitrodiphenyl sulphide with tin and hydrochloric acid.[6] It was recrystallised from methanol and had m. p. 96—97°.

* Part XIX, *J.*, 1956, 1925.

[1] Szmant and Brost, *J. Amer. Chem. Soc.*, 1951, **73**, 4175; Szmant and Lapinski, *ibid.*, 1952, **74**, 4395.
[2] Gillespie, *J.*, 1950, 2542.
[3] Gillespie, Hughes, and Ingold, *J.*, 1950, 2473; Gillespie and Leisten, *J.*, 1954, 1.
[4] Gillespie and Oubridge, *J.*, 1956, 80.
[5] Nietzki and Bothof, *Ber.*, 1894, **27**, 3261.
[6] Bourgeois and Huber, *Rec. Trav. chim.*, 1912, **31**, 30.

Diphenyl sulphoxide, prepared by oxidation of the sulphide with an equimolecular amount of a 30% solution of hydrogen peroxide in glacial acetic acid [7] and recrystallised from ligroin, had m. p. 70·7°.

4-Nitro- and 4 : 4′-dinitro-diphenyl sulphoxide were prepared in the same manner as diphenyl sulphoxide from the corresponding sulphide, and after recrystallisation from ethanol had m. p.s [8] 108—109° and 178°, respectively. The corresponding sulphones were prepared by oxidation with an excess of 30% hydrogen peroxide in glacial acetic acid at 100°.[9] They were recrystallised from acetic acid and had m. p.s [8] 141° and 251°, respectively.

TABLE 1.

| $m_2$ | F. p. (obs.) | F. p. (corr.) | $\theta$ | $\nu'$ | $m_2$ | F. p. (obs.) | F. p. (corr.) | $\theta$ | $\nu'$ |
|---|---|---|---|---|---|---|---|---|---|
| 4-Nitrodiphenyl sulphoxide | | | | | 4 : 4′-Dinitrodiphenyl sulphoxide | | | | |
| 0·00000 | 10·359° | 10·515° | — | — | 0·00000 | 10·365° | 10·515° | — | — |
| 0·01185 | 10·262 | 10·365 | 0·150° | 2·07 | 0·02245 | 10·155 | 10·224 | 0·291° | 2·12 |
| 0·02146 | 10·165 | 10·242 | 0·273 | 2·08 | 0·05061 | 9·837 | 9·874 | 0·641 | 2·07 |
| 0·03413 | 10·026 | 10·082 | 0·433 | 2·07 | 0·08523 | 9·418 | 9·441 | 1·074 | 2·06 |
| 0·04823 | 9·865 | 9·909 | 0·606 | 2·05 | 0·1256 | 8·904 | 8·919 | 1·596 | 2·08 |
| 4-Nitrodiphenyl sulphone | | | | | 4 : 4′-Dinitrodiphenyl sulphone | | | | |
| 0·0000 | 10·365 | 10·515 | — | — | 0·00000 | 10·365 | 10·515 | — | — |
| 0·0430 | 10·089 | 10·163 | 0·352 | 1·34 | 0·01896 | 10·238 | 10·370 | 0·145 | 1·25 |
| 0·0792 | 9·817 | 9·863 | 0·652 | 1·34 | 0·03143 | 10·155 | 10·275 | 0·240 | 1·25 |
| 0·1100 | 9·569 | 9·604 | 0·911 | 1·36 | 0·04125 | 10·074 | 10·184 | 0·331 | 1·31 |
| 0·1280 | 9·419 | 9·450 | 1·065 | 1·36 | 0·04838 | 10·031 | 10·136 | 0·379 | 1·28 |
| 0·1453 | 9·296 | 9·324 | 1·191 | 1·34 | 0·05051 | 9·957 | 10·054 | 0·461 | 1·29 |
| | | | | | 0·06537 | 9·908 | 10·001 | 0·514 | 1·28 |

TABLE 2.

| Time (hr.) | $m_2$ | F. p. (obs.) | F. p. (corr.) | $\theta$ | $\nu'$ | Time (hr.) | $m_2$ | F. p. (obs.) | F. p. (corr.) | $\theta$ | $\nu'$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Diphenyl sulphoxide (Expt. A) | | | | | | Diphenyl sulphoxide (Expt. B) | | | | | |
| — | 0·00000 | 10·365° | 10·580° | — | — | — | 0·0000 | 10·365° | 10·580° | — | — |
| 0·25 | 0·02935 | 9·992 | 10·035 | 0·545° | 3·03 | 0·22 | 0·1007 | 9·110 | 9·123 | 1·457° | 2·35 |
| 0·48 | 0·02935 | 9·961 | 10·004 | 0·576 | 3·17 | 0·52 | 0·1007 | 8·990 | 9·003 | 1·577 | 2·54 |
| 1·42 | 0·02935 | 9·939 | 9·982 | 0·598 | 3·32 | 1·13 | 0·1007 | 8·940 | 8·953 | 1·627 | 2·62 |
| 3·00 | 0·02935 | 9·935 | 9·978 | 0·602 | 3·35 | 2·18 | 0·1007 | 8·855 | 8·868 | 1·712 | 2·76 |
| 4·34 | 0·02935 | 9·931 | 9·974 | 0·606 | 3·37 | 3·32 | 0·1007 | 8·798 | 8·811 | 1·769 | 2·85 |
| 23·2 | 0·02935 | 9·925 | 9·968 | 0·612 | 3·40 | 19·1 | 0·1007 | 8·665 | 8·678 | 1·902 | 3·07 |
| 47·2 | 0·02935 | 9·921 | 9·964 | 0·616 | 3·42 | 23·3 | 0·1007 | 8·655 | 8·668 | 1·912 | 3·08 |
| 4 : 4′-Dinitrodiphenyl sulphide | | | | | | | | | | | |
| — | 0·0000 | 10·359 | 10·515 | — | — | 2 | 0·1011 | 9·256 | 9·281 | 1·234 | 1·99 |
| 0 | 0·0486 | 9·902 | 9·946 | 0·569 | 1·91 | 3 | 0·1251 | 8·997 | 9·017 | 1·498 | 2·00 |
| 1 | 0·0772 | 9·593 | 9·627 | 0·888 | 1·88 | 24 | 0·1251 | 8·837 | 8·858 | 1·657 | 2·21 |
| 4-Aminodiphenyl sulphide (Expt. A) | | | | | | 4-Aminodiphenyl sulphide (Expt. B) | | | | | |
| — | 0·00000 | 10·362 | 10·515 | — | — | — | 0·00000 | 10·365 | 10·515 | — | — |
| 0·26 | 0·02496 | 9·845 | 9·885 | 0·630 | 4·12 | 0·28 | 0·03436 | 9·573 | 9·601 | 0·914 | 4·34 |
| 0·52 | 0·02496 | 9·844 | 9·884 | 0·631 | 4·13 | 2·27 | 0·03436 | 9·562 | 9·590 | 0·925 | 4·40 |
| 1·05 | 0·02496 | 9·840 | 9·880 | 0·635 | 4·16 | 20·1 | 0·03436 | 9·524 | 9·552 | 0·963 | 4·58 |
| 3·8 | 0·02496 | 9·812 | 9·852 | 0·663 | 4·34 | 48·7 | 0·03436 | 9·422 | 9·450 | 1·065 | 5·06 |
| 23·5 | 0·02496 | 9·786 | 9·826 | 0·689 | 4·51 | 120 | 0·03436 | 9·294 | 9·322 | 1·193 | 5·67 |
| 54·5 | 0·02496 | 9·699 | 9·739 | 0·776 | 5·08 | 288 | 0·03436 | 9·259 | 9·287 | 1·228 | 5·84 |
| 200 | 0·02496 | 9·652 | 9·692 | 0·823 | 5·39 | | | | | | |

*Results.*—Table 1 gives the results for those substances that gave stable solutions, as indicated by their time-independent values of $\nu'$, and that could be recovered on dilution of their solutions with water. Table 2 gives the results for those substances that reacted with the solvent. Their $\nu'$ values were time-dependent and they could not be recovered on dilution of their solutions with water. Both Tables give the observed freezing points of the solutions and the freezing points corrected for incomplete repression of the self-ionisation equilibria.[3, 4, 10]

The freezing-point depression $\theta$ is related to the molality of the solute $m_2$ by the equation

$$\theta/m_2 = 6{\cdot}12\,\nu'(1 - 0{\cdot}001959)[1 + (2\varepsilon_2 - \nu_2)m_2/2m_1]$$

[7] Hinsberg, *Ber.*, 1910, **43**, 289.
[8] Szmant and McIntosh, *J. Amer. Chem. Soc.*, 1951, **73**, 4356.
[9] Gilman and Broadbent, *ibid.*, 1947, **69**, 2056.
[10] Flowers, Gillespie, and Oubridge, *J.*, 1956, 1925.

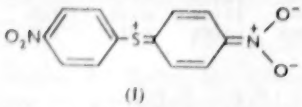
which is equation (2) of Part XIX,[10] where $s_2$ is the number of moles of the solvent reacting with one mole of the solute, and $\nu' = \nu_2 g$ where $\nu_2$ is the number of moles of solute particles formed from one mole of the solute and $g$ is the osmotic coefficient of the solvent. As $g$ is approximately unity,[4,10] $\nu'$ is an approximation to $\nu_2$. The last column in both Tables gives the values of $\nu'$ calculated by means of the above equation. Szmant and Brost [1] present their results in terms of the van't Hoff $i$ factor which is also an approximation to $\nu_2$.

## Discussion

*Sulphides.*—Szmant and Brost [1] found that diphenyl sulphide, dibenzyl sulphide, and 4 : 4'-dinitrodibenzyl sulphide all gave unstable solutions and high time-dependent $i$-values. They also found that the solutions evolved sulphur dioxide and that the original substance could not be recovered on dilution of the solution with water. On the other hand, they found that 4 : 4'-dinitrodiphenyl sulphide apparently gave a stable solution, could be recovered on dilution, and had an $i$-factor of 2·3 (after 11—15 hr.). They took these results to indicate a simple basic ionisation :

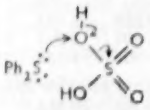
$$(NO_2{\cdot}C_6H_4)_2S + H_2SO_4 = (NO_2{\cdot}C_6H_4)_2SH^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

We have re-investigated the behaviour of 4 : 4'-dinitrodiphenyl sulphide and as may be seen from Table 2 we obtained an initial $\nu'$ value of approximately 1·9 which increased in 24 hr. to approximately 2·2. Thus it seems likely that a simple basic ionisation does occur although, as one might expect the nitro-groups to be ionised to a small extent [2] also, the protonation of the sulphur atom may be incomplete. The basicity of the sulphur may be appreciably reduced by the contribution of resonance structures such as (I). The slow increase of $\nu'$ with time indicates the occurrence of some additional slow reactions such as sulphonation and oxidation. The rates of these reactions are, however, much less than for the unsubstituted sulphide.



(I)

The rate of sulphonation is considerably reduced by the introduction of nitro-groups into the *para*-positions of the aromatic rings as a consequence of their electron-withdrawing properties. The rate of oxidation at the sulphur atom is also considerably decreased and this is consistent with a mechanism for the oxidation such as that involving nucleophilic attack of the sulphur atom on an oxygen atom of the sulphuric acid molecule (reaction 3).



$$\rightarrow \quad Ph_2\ddot{S}{=}O \; + \; SO_2 \; + \; H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

We also investigated the behaviour of 4-aminodiphenyl sulphide, which was found to give initial $\nu'$ values of 4·1 and 4·3 in different experiments which increased to 4·5—4·6 in approximately 24 hr., and to values greater than 5·0 after several days. It seems likely that both the amino-groups and the sulphur atom are protonated and that the unsubstituted ring initially undergoes rather rapid sulphonation, although the reaction becomes slow in its later stages because of the water liberated by the reaction (cf. the following discussion of the sulphonation of sulphoxides). Oxidation probably also occurs. Complete sulphonation and protonation of the sulphur and amino-groups would give a $\nu$ value of 5·0.

$$Ph{\cdot}S{\cdot}C_6H_4{\cdot}NH_2 + 4H_2SO_4 = HO_3S{\cdot}C_6H_4{\cdot}\overset{+}{S}H{\cdot}C_6H_4{\cdot}\overset{+}{N}H_3 + H_3O^+ + 3HSO_4^- \quad . \quad . \quad . \quad (4)$$

*Sulphoxides.*—Szmant and Brost reported that diphenyl sulphoxide gave a constant value of $i$ of 4·8 over a period of 2—20 hr. after addition to sulphuric acid. As may be seen from Table 2 and the Figure, we found that $\nu'$ increases with time, reaching a reasonably constant value of 3·4 after about 2 hr. in expt. A and 3·1 after about 10 hr. in expt. B. The colour of the solution faded from a deep green to a pale blue-green as the freezing point decreased. Contrary to the observations of Szmant and Brost, who claimed that diphenyl sulphoxide could be recovered unchanged on dilution of its sulphuric acid solution, we found

that only a very small precipitate, insufficient to identify with certainty, was obtained on diluting a solution after its freezing point had become approximately constant.

Our results do not therefore support Szmant and Brost's conclusion that the diphenylsulphidonium ion $Ph_2S^{++}$ is formed according to equation (1), since this requires a constant $\nu$ value of 5 and complete recovery on dilution according to the equation :

$$Ph_2S^{++} + 3H_2O = Ph_2S{:}O + 2H_3O^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

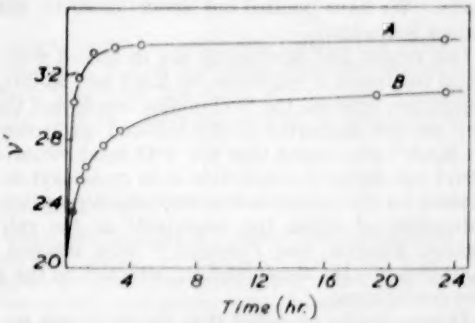
Our observations may be reasonably explained by assuming that there is an initial protonation of the sulphoxide group

$$Ph_2SO + H_2SO_4 = Ph_2S{:}OH^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

giving an initial $\nu$ value of 2·0 which is followed by a rather rapid sulphonation in one of the aromatic rings,

$$Ph_2S{=}OH^+ + 2H_2SO_4 = HO_3S{\cdot}C_6H_4{\cdot}SPh{=}OH^+ + H_3O^+ + HSO_4^- \quad . \quad . \quad . \quad . \quad (7)$$

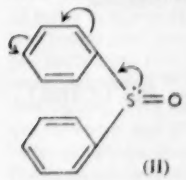
which on completion would give a $\nu$ value of 4. The initial increase in $\nu'$ is very rapid and our $\nu'$–time curves cannot therefore be reliably extrapolated to zero time, but they are consistent with an initial $\nu'$ value of 2·0 and they have been extrapolated to this value in the Figure. The fact that the sulphonation apparently stops or at least becomes very slow




*Variation of $\nu'$ for diphenyl sulphoxide with time.*

before completion may be attributed to the water formed in the reaction since the rate of sulphonation is known to decrease very rapidly with increasing concentration of water in the region of 100% $H_2SO_4$.[11] In the more concentrated solution (expt. B) the initial reaction is slower and the limiting value of $\nu'$ is smaller than in the more dilute solutions (expt. A). Both these observations are consistent with a greater change in the solvent composition in the more concentrated solution corresponding to the larger amount of water liberated by the sulphonation.

Diphenyl sulphoxide is sulphonated much more readily than diphenyl sulphone which is quite stable in sulphuric acid at room temperature. Presumably the deactivating inductive effect of the sulphoxide group is counterbalanced by the conjugation of the unshared pair of electrons on the sulphur with the aromatic ring (II).[12] (The conjugation of the S=O double bond with the aromatic ring appears to be rather slight.[12,13])




(II)

The introduction of a nitro-group into one of the aromatic rings is apparently sufficient to deactivate both rings towards sulphonation, as 4-nitrodiphenyl sulphoxide gave a stable pink solution and a constant $\nu'$ value of 2·07 which is presumably due mainly to protonation of the sulphoxide group. Some protonation of the nitro-group would be expected,[2] but the actual contribution that this makes to the observed $\nu'$ value cannot be found from the cryoscopic measurements. The colour of the solution of 4-nitrodiphenyl sulphoxide in

[11] Cowdrey and Davies, *J.*, 1949, 1871.
[12] Koch, *J.*, 1950, 2892.
[13] Koch and Moffitt, *Trans. Faraday Soc.*, 1951, **47**, 7.

sulphuric acid deepened considerably at room temperature during several days. As this colour change was not accompanied by any change in the freezing point of the solution, it cannot be due to change in the total number of solute particles. We cannot offer any explanation of this observation. 4 : 4′-Dinitrodiphenyl sulphoxide gave an orange solution and a constant $v'$ value of 2·04, which is not significantly different from that given by 4-nitrodiphenyl sulphoxide. Again the colour of the solution deepened and after several days was deep red. The observed $v'$ value is presumably due to extensive protonation of the sulphoxide group together with a small amount of protonation of the nitro-groups.

*Sulphones.*—Our present results extend the earlier work of Gillespie,[2] who obtained a $v'$ value for diphenyl sulphone of 1·20. It may be seen from Table 1 that the introduction of a nitro-group into the *para*-position of one of the aromatic rings causes $v'$ to increase to 1·35 and the introduction of a second nitro-group into the *para*-position of the other ring causes a slight decrease to 1·28. Both substances gave pale yellow solutions and could be recovered on dilution with water. These results are consistent with the interpretation that the sulphone group is partially protonated and that the nitro-groups are slightly protonated and reduce the basicity of the sulphone group to some extent.

Our results do not agree with those obtained by Szmant and Brost who found $i$-values of 1·5 for 4-nitrodiphenyl sulphone and 2·0 for 4 : 4′-dinitrodiphenyl sulphone and postulated that nitro-groups increase the basicity of the sulphone group in order to explain their results. We have pointed out above, however, that the accuracy of Szmant and Brost's $i$ values is doubtful.

Our results and conclusions are in accord with the results of a theoretical molecular-orbital treatment of sulphones by Koch and Moffitt,[13] who showed that there is only slight conjugation between the S=O double bonds and the aromatic rings in diphenyl sulphone. They are also supported by the infrared spectroscopic measurements of Barnard, Fabian, and Koch,[4] who found that the S=O bond vibration frequencies are the same in methyl phenyl and diphenyl sulphoxide as in *cyclo*hexyl methyl sulphoxide. A similar result was obtained for the corresponding sulphone derivatives. They concluded that there was little conjugation of either the sulphoxide or the sulphone group with the aromatic rings. Leandri, Mangini, and Passerini [15] have reached a similar conclusion from ultraviolet absorption spectra measurements, although in the photo-excited state there appears to be more conjugation.

It may finally be noted that the sulphones we have studied are considerably weaker bases than the corresponding sulphoxides. Barnard, Fabian, and Koch [14] have shown that sulphoxides form stronger hydrogen bonds than sulphones and they attribute this to the greater basicity of sulphoxides. They also found on the basis of force constants that the S=O bond in sulphoxides is weaker than in sulphones. These observations are in accord with the view that, because of the greater electronegativity of the sulphur atom in sulphones than in sulphoxides, the bonds in the former are less polar and stronger than in the latter. The greater resulting negative charge on the oxygen atom of the sulphoxides than on the oxygen atoms of sulphones accounts for the greater basicity of the former.

We thank Mr. J. V. Oubridge for carrying out the cryoscopic measurements on 4-aminodiphenyl sulphide, and Professor C. K. Ingold, F.R.S., for helpful advice and criticism.

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[*Received, May 1st,* 1956.]

[14] Barnard, Fabian, and Koch, *J.*, 1949, 2442.
[15] Leandri, Mangini, and Passerini, *Gazzetta*, 1954, **84**, 73.

## 749. *The Thermal Decomposition of* cyclo*Pentyl Bromide.*

By S. J. W. Price, R. Shaw, and A. F. Trotman-Dickenson.

The thermal decomposition of *cyclo*pentyl bromide into *cyclo*pentene and hydrogen bromide has been studied in a static system at temperatures between 300° and 360° c. The decomposition is homogeneous and obeys first-order kinetics in its early stages; the rate constant is given by

$$k = 10^{11\cdot9}\exp(-41{,}400/RT)\ \text{sec.}^{-1}$$

The elimination of hydrogen bromide is probably a molecular process, as the addition of *cyclo*hexene has no effect upon the rate.

During the past few years the thermal decomposition of many aliphatic bromides has been investigated, chiefly by Maccoll and his collaborators.[1,2] The majority of these bromides, in the presence of an inhibitor, decompose by a four-centre molecular elimination mechanism into hydrogen bromide and an olefin. One of the compounds which has been found to react in this way is *cyclo*hexyl bromide.[3] The rate constant for its decomposition is given by the Arrhenius equation

$$k = 10^{13\cdot5}\exp(-46{,}100/RT)\ \text{sec.}^{-1}$$

The investigation of the decomposition of *cyclo*pentyl bromide was undertaken in the hope that a knowledge of the rate factors, $A$ and $E$ in the Arrhenius equation, would throw light on the features of molecules which determine the rates of molecular elimination reactions. In particular, it was thought that the different degrees of flexibility of the carbon rings might influence the rates.

### Experimental

*Materials.*—The *cyclo*pentyl bromide was a gift from the Michigan Chemical Company. It was degassed and purified by bulb-to-bulb distillation. No significant quantities of impurity could be detected by vapour-phase chromatography. The *cyclo*hexene, which was similarly degassed, was freed from peroxides by shaking with acid ferrous sulphate solution.

*Apparatus.*—The decomposition was studied in a bulb of 385 c.c. capacity attached to a conventional vacuum-system by tubing with a total dead space of approx. 13 c.c. The bulb was contained in a mercury-vapour jacket, whose temperature could be readily controlled by varying the pressure under which the mercury boiled. The temperature of the jacket was determined by reference to standard tables of the vapour pressure of mercury. The reaction was studied by following the change in pressure in the reaction vessel on a mercury manometer. It was found that the hydrogen bromide formed did not appreciably attack the mercury during a run, for the reaction vessel was separated from the manometer by about 30 cm. of 2-mm. capillary tubing.

*Procedure.*—Runs were started by admitting a suitable quantity of the bromide to the reaction vessel from a storage bulb; in some runs a quantity of *cyclo*hexene was also added. Readings of the pressure in the vessel were then recorded at convenient intervals. At the end of some of the runs the quantity of hydrogen bromide formed was determined analytically. It was found that inexplicably erratic and high results were usually obtained when the unseparated products were titrated with alkali, so the following procedure was adopted. First, the products were condensed in a side bulb, and the hydrogen bromide was separated by low-temperature distillation. Its amount was then determined by pressure measurements and by dissolving the gas in water and titrating the solution for hydrogen and halide ions. The results of the three determinations were always in excellent agreement. When a proper correction was made for the dead space it was found that the analytical results agreed well with degrees of decomposition deduced from the pressure measurements.

Rate constants were determined in the usual way from first-order plots of the logarithms of

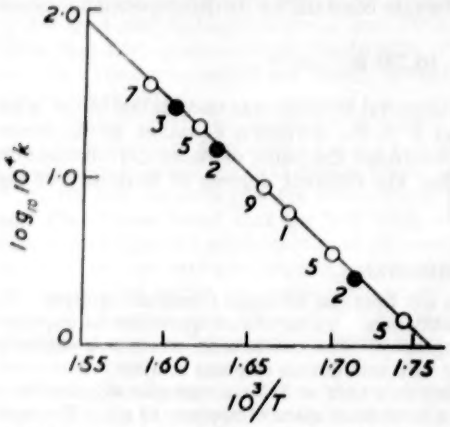
[1] Harden and Maccoll, *J.*, 1955, 2454, and ref. 4.
[2] For similar reactions, see Trotman-Dickenson, "Gas Kinetics," Butterworths, London, 1955.
[3] Green and Maccoll, *J.*, 1955, 2449.

the pressure changes against time. The logarithmic plots were strictly linear for the first third of the reaction but thereafter tended to curve. The curvature was probably caused by the increasing importance of the back reaction. The rate constants for a few runs were calculated from the full expression for a first-order reaction opposed by a second-order reaction. The rate constants obtained in this way differed by only about 10% from those calculated by applying the equation for a simple first-order reaction to the observations made during the first third of the decomposition. All the rate constants reported here were determined by the less tedious procedure.

All runs showed short induction periods. Their lengths corresponded roughly to the time needed for 2—3% of the bromide to decompose. The presence of *cyclo*hexene appeared to shorten the induction periods slightly.

## Results and Discussion

Preliminary runs in a clean-walled reaction vessel gave first-order rate constants which decreased slowly but steadily from run to run. Maccoll and his collaborators observed similar behaviour with other bromides and attributed the effect to heterogeneous processes. They therefore seasoned their reaction vessels by decomposing allyl bromide in them. This




*Arrhenius plot for the thermal decomposition of* cyclo*pentyl bromide.*
○ Unpacked reaction vessel.
● Packed reaction vessel.
The figures by the circles indicate the number of runs averaged to obtain each point.

remedy proved effective for *cyclo*pentyl bromide also. It was used after any occasion on which air had been admitted to the reaction vessel. Incidentally, Maccoll's rate constant [4] for the decomposition of allyl bromide was confirmed.

The first-order nature of the decomposition was demonstrated by studying it with various initial pressures of *cyclo*pentyl bromide. The results obtained for a typical series of runs, all corrected to 356·5°, were as follows :

| Initial pressure (mm.) | 38·0 | 49·6 | 59·6 | 79·5 | 94·0 | 105·0 | 107·5 |
|---|---|---|---|---|---|---|---|
| $10^4k$ (sec.$^{-1}$) | 3·48 | 3·48 | 3·39 | 3·66 | 3·53 | 3·80 | 3·78 |

The very small effect on the rate constant of the addition of *cyclo*hexene can be seen from the following Table, in which the observed rate constants are compared with those calculated from the Arrhenius equation. The variations in the rates are of the same order as the experimental error.

| *cyclo*Hexene (mm.) | 20·0 | 30·0 | 10·0 | 9·0 | 40·0 |
|---|---|---|---|---|---|
| *cyclo*Pentyl bromide (mm.) | 60·0 | 72·5 | 64·0 | 48·2 | 38·0 |
| Temp. | 300·7° | 315·2° | 331·3° | 344·5° | 365·5° |
| $k$ (obs.)/$k$ (calc.) | 1·05 | 0·95 | 1·02 | 0·98 | 0·91 |

Seven runs were carried out with the reaction vessel packed with Pyrex tubing so that the surface/volume ratio was increased from 0·9 to 2·0 cm.$^{-1}$. The results of these runs are distinctively plotted alongside the other results in the Figure. It can be seen that there is no evidence for any heterogeneous contribution to the reaction in an aged vessel.

[4] Maccoll, *J.*, 1955, 965.

The results of all the runs are shown on an Arrhenius plot in the Figure. The Arrhenius equation was derived by a least-squares treatment of the results for all the individual runs. The results are best expressed by the equation :

$$k = 10^{11\cdot9}\exp(-41{,}400/RT)\ \text{sec.}^{-1}$$

Our experiments indicate that this is the rate constant for the homogeneous gas-phase molecular elimination of hydrogen bromide from *cyclo*pentyl bromide.

The rate constant for this decomposition at 380° (0·010 sec.$^{-1}$) is very slightly greater than that (0·008 sec.$^{-1}$) for the similar decomposition of *cyclo*hexyl bromide. This conclusion is of interest in view of a recent important suggestion [5] that the rate constants for the molecular elimination of hydrogen bromide from aliphatic bromides should run parallel to the rate constants for the elimination of bromide ions from the bromides by the $S_N1$ mechanism. No measurements on the rates of the $S_N1$ reactions of *cyclo*pentyl and *cyclo*hexyl bromide have been reported. It has been found,[6] however, that the $S_N1$ reaction of 1-methyl*cyclo*pentyl chloride in 80% aqueous ethanol at 25° is 125 times more rapid than the corresponding reaction of 1-methyl*cyclo*hexyl chloride. Evidently the parallelism between the rates of the $S_N1$ reactions and the molecular eliminations breaks down in this instance. Probably the cause is the different natures of the strains in the two types of transition states.

THE UNIVERSITY, EDINBURGH 9. [*Received, May 30th*, 1956.]

[5] Maccoll and Thomas, *Nature*, 1955, **176**, 392.
[6] Brown and Borkowski, *J. Amer. Chem. Soc.*, 1952, **74**, 1894.

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## 750. *Intramolecular Acylation. Part I. Ring Closure of Some β-(7-Alkyl-1-naphthyl)propionic Acids.*

By A. J. M. WENHAM and J. S. WHITEHURST.

Cyclisation of β-7-methyl-, β-7-ethyl-, and β-7-*iso*propyl-1-naphthylpropionic acids and of their acid chlorides gives only the products of *peri*-ring closure.

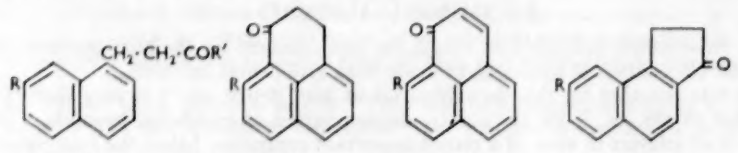
CYCLISATION of β-1-naphthylpropionic acid (I; R = H, R′ = H) can be made to yield perinaphthan-1-one (II), perinaphthen-1-one (III), or 4 : 5-benzindan-1-one (IV).[1] The present investigation concerned the effect of a 7-substituent, and this paper presents the results obtained with the methyl, ethyl, and *iso*propyl compounds. We also investigated the preparation of the methoxy-acid (I; R = OMe) but discontinued it when a paper by Hey and Green [2] appeared.

All the syntheses started from the readily available tetralones (V; R = Alkyl). Clemmensen reduction of the β-*p*-alkylbenzoylpropionic acids to the butyric acids [the precursors of (V)] was, in our hands, more tedious and less reliable than the Wolff–Kishner reduction (Huang-Minlon modification). Cyclisation of the butyryl chlorides by a modification of the method of Newman, Anderson, and Takemura [3] gave the tetralone in over 90% yield.

The first attempts to complete the synthesis involved conversion of 7-methoxy-1-tetralone into 1-formyl-1 : 2 : 3 : 4-tetrahydro-7-methoxynaphthalene. Unfortunately, the initial Darzens condensation gave only a viscous yellow oil (containing much unchanged tetralone) which did not appear to undergo hydrolysis under Claisen conditions,[4] but did

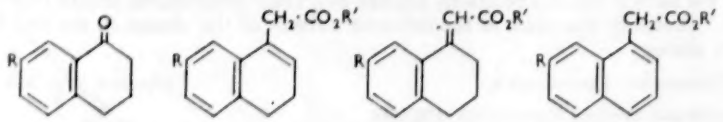
[1] (*a*) Mayer and Sieglitz, *Ber.*, 1922, **55**, 1835; von Braun, Manz, and Reinsch, *Annalen*, 1929, **468**, 277; Darzens and Levy, *Compt. rend.*, 1935, **201**, 902; Buu-Hoï and Cagniant, *ibid.*, 1943, **216**, 346; (*b*) Cook and Hewett, *J.*, 1934, 365; (*c*) Fieser and Gates, *J. Amer. Chem. Soc.*, 1940, **62**, 2335.
[2] Hey and Green, *J.*, 1954, 4306.
[3] Newman, Anderson, and Takemura, *J. Amer. Chem. Soc.*, 1953, **75**, 347; cf. Bachmann and Horton, *ibid.*, 1947, **69**, 58.
[4] Claisen, *Ber.*, 1905, **38**, 693; Johnson, Belew, Chinn, and Hunt, *J. Amer. Chem. Soc.*, 1953, **75**, 4995.

yield an acid on more vigorous treatment. Decarboxylation of this acid proceeded poorly, yielding no detectable aldehyde. It is noteworthy that benzosuberone is reported to undergo a Darzens condensation normally.[5]




(I) (II) (III) (IV)

The second attempt was a modified Reformatsky reaction involving the tetralone and methyl β-bromopropionate as for the similar case of 6-methoxy-1-tetralone.[6] Whereas the latter yielded 30%, our compound gave less than 10% of the desired product. Hey and Green [2] also report a low yield for this reaction.




(V) (VIa) (VIb) (VII)

The remaining compounds (I; R′ = H) were prepared from the tetralones by means of the Reformatsky reaction and homologation. Ruzicka and Hofmann [7] prepared the methyl derivative (VI*a* or *b*; R = Me, R′ = Et). Our Reformatsky reactions, effected in ether–benzene,[8] required extreme precautions in drying in order to avoid predominant formation of neutral, low-boiling oils. Dehydration of the hydroxy-esters formed was achieved with hot 90% formic acid,[9] and hydrolysis then furnished the acids (VI). Of these only the methyl and ethyl derivatives gave pure compounds (VI*a* or *b*) on crystallisation.

After exploratory experiments, dehydrogenation of the dihydronaphthylacetic acids (VI; R′ = H) was achieved with palladium–charcoal (on a small scale) or, best, by heating the methyl esters with sulphur at 240°. Overall yields from the tetralones to the naphthylacetic acids were 34—41%. The naphthylacetyl chlorides were fairly readily cyclised to the corresponding acenaphthenones by aluminium chloride but not by stannic chloride. Polyphosphoric acid failed to cyclise the free acids. In the Arndt–Eistert chain-lengthening of acids (VII; R′ = H), Newman and Beal's [10] improvement of the Wolff rearrangement gave 40—62% yields.

The two main types of cyclisation were examined, *viz.*, cyclodehydration by acid, and internal Friedel–Crafts reaction on the acid chlorides. During separation and purification of the products by chromatography on alumina, prolonged contact with the absorbent and exposure to strong light had to be avoided as both caused much decomposition. The initial products from these reactions must be either perinaphthanones (II) or benzindanones (IV). Such compounds differ sufficiently in ultraviolet light absorption to be characterised.[2,11] Thus for ethanol solutions perinaphthanones show maximum absorption at 248, 322, and 331 mμ whereas benzindanones have peaks at 250, 275, 284, 294, 331, and 334 mμ. Moreover, the former on dehydrogenation should yield perinaphthenones (III), which besides being soluble in, and recoverable from, aqueous mineral acid [10]

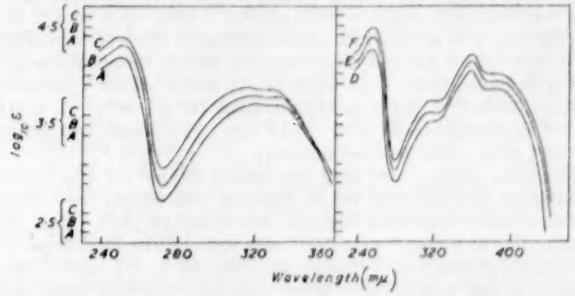
[5] Horton and Walker, *ibid.*, 1952, **74**, 758.
[6] Haberland and Heinrich, *Ber.*, 1939, **72**, 1222.
[7] Ruzicka and Hofmann, *Helv. Chim. Acta*, 1937, **20**, 1155.
[8] Cf. Bachmann, Cole, and Wilds, *J. Amer. Chem. Soc.*, 1940, **62**, 824.
[9] Johnson and Glenn, *ibid.*, 1949, **71**, 1087.
[10] Newman and Beal, *ibid.*, 1950, **72**, 5163.
[11] Ansell and Berman, *J.*, 1954, 1792.

have a characteristic band at 358 mμ.[11,12] It is perhaps conceivable that benzindanones could be converted into benzindenones [isomers of (III)] under conditions described in this work. However, such compounds, unsubstituted in the *cyclo*pentadienone ring, should be very unstable. Indenone [13] itself rapidly polymerises to a colourless high-melting product on storage or in contact with mineral acids. The properties of our dehydro-compounds can only be accounted for by a perinaphthenone structure.

The reaction between polyphosphoric acid and β-(7-methyl-1-naphthyl)propionic acid at 140° (45 minutes) furnished 9-methylperinaphthenone as sole product, whereas at 110—120° (15 minutes) the chief product was the perinaphthanone. The latter conditions were extended to the other two acids with similar results. 85% Sulphuric acid gave only water-soluble material. Anhydrous hydrogen fluoride gave the alkylperinaphthanones in very high yields (87—94%) along with traces of the perinaphthenones.

Aluminium chloride with ethylene chloride solutions of the acid chlorides at 15° furnished only (74—96%) the perinaphthanones, but yields fell to 57—81% when nitrobenzene was used as solvent. The stannic chloride method, giving 90—93% yields of perinaphthanones, was the preparative reaction of choice. Chromatography and spectrographic examination showed that not more than traces of the isomeric benzindanones

*Light absorption, in* EtOH, *of*: FIG. 1, 9-*methyl-* (*curve A*), 9-*ethyl-* (*B*), *and* 9-*iso*propyl-*perinaphthanone* (*C*); FIG. 2, 9-*methyl-* (*D*), 9-*ethyl-* (*E*), *and* 9-*iso*propyl-*perinaphthenone* (*F*).




For FIG. 2 (right) the vertical scales for curves *D*, *E*, and *F* correspond to those for curves *A*, *B*, and *C*, respectively, in FIG. 1 (left).

could have been formed. This is surprising as β-1-naphthylpropionic acid (I; R = H, R′ = H), treated with stannic chloride [15] or hydrogen fluoride,[1c] gives a small yield of benzindanone (IV; R = H). Evidently, the electron-releasing properties of the alkyl groups outweigh their steric effect.

Few examples of deliberate dehydrogenations of perinaphthanones have been cited. Ansell and Berman,[11] having regard to the incidental dehydrogenation which often accompanies cyclisations with aluminium chloride–nitrobenzene, treated some 3-alkyl-perinaphthanones in this way and obtained small yields of the desired product. Loudon and Razdan [14] used palladium–charcoal on 9-hydroxyperinaphthan-1-one. In our work palladium–charcoal, alone or in the presence of *cyclo*hexane, had little effect on 9-methyl-perinaphthan-1-one. The 9-ethyl isomer behaved similarly but with the same catalyst in hot trimethylene glycol [15] it gave a 34% yield of dehydro-product. As 9-methyl-perinaphthen-1-one had been formed by a cyclisation in hot polyphosphoric acid, it was considered likely that the latter might dehydrogenate the perinaphthanone. This was the case, the yield (13%) being doubled on addition of palladium–charcoal. If the acidity of the medium is an important factor, then the use of the still stronger trichloroacetic acid should enhance the process and it was found that yields were increased thus to 33—65%. The best of the methods tried was the dehydrobromination of the 2-bromo-derivatives

[13] Cromwell and Hudson, *J. Amer. Chem. Soc.*, 1953, **75**, 872.
[14] Marvel and Hinman, *ibid.*, 1954, **76**, 5435.
[15] Loudon and Razdan, *J.*, 1954, 4299.
[15] Leonard and Berry, *J. Amer. Chem. Soc.*, 1953, **75**, 4989.

of these perinaphthanones. During bromination in carbon tetrachloride orange precipitates appeared, probably related to the dibromoperinaphthenones investigated by Lukin,[16] but these disappeared when the solutions were boiled. Evaporation and treatment with triethylamine gave the perinaphthenones in 46—78% yield.

## Experimental

*Aroylpropionic Acids.*—Finely powdered anhydrous aluminium chloride (240 g., 1·8 moles) was added to a stirred mixture of the hydrocarbon (0·88 mole), succinic anhydride (80 g., 0·8 mole), and tetrachloroethane (300 ml.). After 3 hr. at room temperature the mixture was poured on ice and hydrochloric acid, and the organic layer washed and steam-distilled. Dissolution of the crude acids in sodium carbonate solution followed by precipitation with mineral acid gave 86—92% of slightly impure products, and crystallisation from benzene afforded 72—77% of pure materials.

*γ-p-Tolylbutyric Acid.*—β-*p*-Toluoylpropionic acid (109·5 g.), potassium hydroxide (96 g.), 90% w/w hydrazine hydrate (76 ml.), and ethylene glycol (500 ml.) were refluxed for 3 hr., distilled until the temperature had risen to 198°, and refluxed again for a further 12 hr. Working up in the usual way gave γ-*p*-tolylbutyric acid (82·9 g., 82%), b. p. 144—146°/1 mm., m. p. 60—62°. Analogous compounds were prepared in a similar manner.

*7-Methyltetralone.*—γ-*p*-Tolylbutyric acid (82·9 g., 0·465 mole) in benzene (200 ml.) was added to phosphorus pentachloride (127 g., 0·613 mole) under benzene (200 ml.). After 15 min. the solution was warmed on the water-bath for 5 min, then cooled to 0°. Anhydrous stannic chloride (132 ml., 1·05 moles) was added rapidly to the well-stirred solution (frothing) and after 6 hr. the dark brown solution was poured on ice and hydrochloric acid. The benzene layer was washed with hydrochloric acid–water (1 : 1), water, dilute aqueous alkali, and water, dried ($MgSO_4$), and distilled, giving 7-methyltetralone (67 g., 90%), b. p. 122—124°/1 mm., m. p. 34—36°. 7-Ethyltetralone (b. p. 95°/0·18 mm., 92%) and 7-*iso*propyltetralone (b. p. 98°/0·1 mm., 32—36°, 92%) were obtained similarly.

*Reformatsky Reactions.*—Apparatus used was heated at 120° for 4 hr. before use. Zinc foil, cleaned with sand-paper and cut into 1/8 in. squares, was etched with 6N-hydrochloric acid, washed with distilled water and with acetone, and dried at 120°. Pure benzene and pure ether, prepared according to Fieser,[17] were dried with sodium wire for 2 days before use.

To a boiling stirred mixture of 7-methyltetralone (32 g., 0·2 mole), zinc (20 g.), methyl bromoacetate (10 ml.), and 1 : 1 benzene–ether (400 ml.) a crystal of iodine was added, and at intervals of 20 min. two further additions of zinc (20 g.) and methyl bromoacetate (8 ml., 10 ml.), together with a crystal of iodine. After 12 hours' refluxing the precipitated complex was decomposed by 50% aqueous acetic acid (60 ml.), the organic layer was washed with water, saturated sodium hydrogen carbonate solution, water, and saturated brine, dried ($MgSO_4$), and evaporated.

The crude oily hydroxy-ester was refluxed for 30 min. with 90% formic acid (65 ml.), the latter then removed at reduced pressure, and the residue washed in ether with water and dilute sodium hydroxide solution. The ether extract (A) was evaporated and the residue heated for 3½ hr. with 10% (w/v) potassium hydroxide in aqueous methanol (1 : 1) (180 ml.). The methanol was then distilled off at reduced pressure, and the solution diluted with water (2 vol.), and extracted with ether, the extract being rejected. Acidification gave the mixed unsaturated acids as a tan solid (23 g., 57%). Crystallisation from ether–light petroleum (b. p. 40—60°) gave an *acid* as colourless needles, m. p. 84—85° (Found : C, 77·3; H, 6·8. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%).

Distillation of the extract (A) gave a small forerun of colourless neutral oil, b. p. 80—125°/0·4 mm., and then unsaturated ester (26·5 g., 61·4%), b. p. 128—132°/0·4 mm.

Similar reactions with 7-ethyl- and 7-*iso*propyl-tetralone gave crude mixed acids in yields of 70 and 72% respectively. In the case of the ethyl compound, crystallisation from *n*-hexane furnished an unsaturated *acid* as colourless needles, m. p. 81—83° (Found : C, 77·6; H, 7·3. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·5%).

*7-Methyl-1-naphthylacetic Acid.*—The dehydrated, distilled ester (47 g.) from the Reformatsky reaction was heated with sulphur (6·9 g.), the temperature being raised from 210° to 270° during 3¼ hr. The product was taken into ether and washed with 2N-sodium hydroxide

[16] Lukin, *Bull. Acad. Sci. U.R.S.S.*, 1941, 565, 695; *Chem. Abs.*, 1943, **37**, 2734.
[17] Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, 1941.

and water, then dried ($MgSO_4$). Distillation yielded a liquid (38·0 g.), b. p. 117—121°/0·3 mm., which was hydrolysed with boiling 20% aqueous potassium hydroxide (190 ml.) After ether-extraction the aqueous solution was acidified, yielding the crude acid (31·9 g.), m. p. 150—160°. Crystallisation from benzene furnished **7-*methyl*-1-*naphthylacetic acid*** (27·8 g., 64%) as colourless rhombs, m. p. 160—163°. A specimen, further crystallised, had m. p. 164—165° (Found: C, 77·6; H, 5·8. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·0%).

7-*Ethyl*- and 7-iso***propyl*-1-*naphthylacetic acid*** were obtained similarly, as rhombs (from benzene), m. p. 139—141° (Found: C, 78·7; H, 6·8. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%), and needles (from *cyclo*hexane–benzene), m. p. 126—127·5°, respectively (Found: C, 78·8; H, 7·2. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·1%). The latter was obtained in 57% yield by heating the distilled dehydrated Reformatsky ester (23·2 g.) with 25% palladium–charcoal (4·6 g.) under nitrogen at 230—270° and working up in the usual way. The yields of methyl and ethyl compound by this method were lower (25—36%).

β-(7-*Methyl*-1-*naphthyl*)*propionic Acid*.—7-Methyl-1-naphthylacetic acid (27·8 g.) was refluxed with thionyl chloride (30 ml.) and anhydrous ether (170 ml.) containing a drop of pyridine. The solvent and excess of reagent were removed under reduced pressure and the residue was freed from sulphur compounds by repeated evaporation with benzene. The acid chloride was added in ether (50 ml.) dropwise to stirred ice-cold ethereal diazomethane (from 63 g. of methylnitrosourea). Next day, removal of the solvent under reduced pressure at 20—30° left the crude diazo-ketone as yellow crystals, m. p. 65—80° (decomp.), which were dissolved in absolute methanol (320 ml.) and treated with 10 ml. portions of a solution of silver benzoate (10 g.) in dry triethylamine (60 ml.). Reaction was not entirely homogeneous, most of the nitrogen being evolved from the precipitate. After being left overnight the mixture was refluxed for 10 min., filtered, and evaporated. The residue was taken up in ether, washed with N-nitric acid, water, and sodium hydrogen carbonate solution, and dried ($MgSO_4$). Distillation gave methyl β-(7-methyl-1-naphthyl)propionate (21·6 g.), b. p. 140—146°/0·5 mm. Hydrolysis with 20% aqueous potassium hydroxide (110 ml.) and acidification gave the acid which from benzene afforded colourless plates (16·27 g.), m. p. 135—138°. The pure *acid* had m. p. 139—140° (Found: C, 78·2; H, 6·7. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%). β-(7-*Ethyl*-1-*naphthyl*)*propionic acid* (19·8 g., crude) was obtained similarly from the corresponding naphthylacetic acid (39·8 g.), and had m. p. 121·5—123° (from benzene) (Found: C, 79·0; H, 7·2. $C_{15}H_{16}O_2$ requires C, 79·0; H, 7·1%).

7-*iso*Propyl-1-naphthylacetic acid (15·2 g.) furnished the corresponding ester (9·7 g.), b. p. 146—152°/0·3 mm., hydrolysed to the *acid*, needles (8·58 g., crude), m. p. 130—131° (from *cyclo*hexane) (Found: C, 79·3; H, 7·6. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·5%).

*Cyclisation of the Naphthylacetic Acids*.—Details of the acenaphthenones are shown in Table 1. They were crystallised from *cyclo*hexane.

TABLE 1. *Acenaphthenones.*

| | | Found (%) | | | Required (%) | |
|---|---|---|---|---|---|---|
| Deriv. | Form | M. p. | C | H | Formula | C | H |
| 8-Me | Plates | 92—92·5° | 85·6 | 5·5 | $C_{13}H_{10}O$ | 85·7 | 5·5 |
| 8-Et | Needles | 79—80 | 85·7 | 6·2 | $C_{14}H_{12}O$ | 85·7 | 6·2 |
| 8-Pr$^i$ | ,, | 113—114 | 85·4 | 6·4 | $C_{15}H_{14}O$ | 85·7 | 6·7 |

8-*Methylacenaphthenone*. (1) 7-Methyl-1-naphthylacetic acid (0·2 g.) was converted into the acid chloride with thionyl chloride (0·5 ml.) in ether (5 ml.) containing a trace of pyridine. The residue, after removal of solvents and excess of reagent, was dissolved in benzene (6 ml.) and stirred with aluminium chloride (0·15 g.) for 2½ hr. at room temperature. After chromatography on alumina there was isolated 8-methylacenaphthenone (76 mg., 42%), m. p. 82—85°.

(2) Reaction of the above but in nitrobenzene yielded 25 mg., m. p. 91—92°.

(3) Cyclisation of the acid chloride from the acid (1 g.) with aluminium chloride (0·73 g.) in ethylene dichloride (25 ml.) (2 hr.) gave a solid (0·62 g.) purified by chromatography on alumina and collected in fractions (*a*) 0·13 g., m. p. 85—90°, and (*b*) 0·23 g., m. p. 91—92°.

8-*Ethylacenaphthenone*. 7-Ethyl-1-naphthylacetic acid (0·2 g.), converted into the acid chloride and treated with aluminium chloride (0·2 g.) in benzene (3 ml.), yielded 70 mg. (36%) of the acenaphthenone.

8-iso*Propylacenaphthenone* was prepared similarly (25%).

*Cyclisation of the Naphthylpropionic Acids*.—Details of the perinaphthanones are contained in Table 2. The first two were crystallised from light petroleum. 9-iso*Propylperinaphthanone*,

purified by two passages in light petroleum solution (b. p. 40—60°) through alumina, had $n_D^{20}$ 1·6172.

(A) *With polyphosphoric acid* (85% $P_2O_5$). (1) β-(7-Methyl-1-naphthyl)propionic acid. (*a*) The acid (0·5 g.) and the reagent (5 g.) were heated together at 140°. The acid formed a molten layer on the surface at this temperature. The reagent layer was red after 3 min., brown after 15 min., and dark brown after 45 min. The mixture was cooled, then quenched with water, and the organic material isolated with benzene, yielding 0·40 g. of dark oil. Chromatography in benzene on alumina (16 × 1·3 cm.) gave yellow crystals (0·18 g.) which from *cyclo*hexane (charcoal) furnished yellow flakes of 9-*methylperinaphthenone*, m. p. 91—93° (Found: C, 86·1; H, 5·0. $C_{14}H_{10}O$ requires C, 86·6; H, 5·2%).

TABLE 2. *Perinaphthanones.*

| | | | Found (%) | | | Required (%) | |
|---|---|---|---|---|---|---|---|
| Deriv. | Form | M. p. | C | H | Formula | C | H |
| 9-Me | Prisms | 39—41° | 85·1 | 6·1 | $C_{14}H_{12}O$ | 85·7 | 6·2 |
| 9-Et | Plates | 61·5—62·5 | 85·3 | 7·0 | $C_{15}H_{14}O$ | 85·7 | 6·7 |
| 9-Pr$^i$ | Oil | — | 86·0 | 7·3 | $C_{16}H_{16}O$ | 85·7 | 7·2 |

(*b*) The acid (0·5 g.) and reagent (11·5 g.) were heated at 118° for 10 min. The crude product was chromatographed on alumina, yielding 9-*methylperinaphthanone* (0·22 g., 48%), m. p. 33—39°.

(2) β-(7-Ethyl-1-naphthyl)propionic acid. The acid (0·5 g.) was treated as in 1(*b*). 9-*Ethylperinaphthanone* (0·20 g.), m. p. 56—62·5°, was obtained.

(3) β-(7-*iso*Propyl-1-naphthyl)propionic acid. This was heated (0·5 g.) with polyphosphoric acid as already described but for 20 min., and afforded 9-*iso*propylperinaphthanone (0·15 g.).

(B) *With stannic chloride on the acid chloride.* The requisite acid (usually 0·5 g.) was converted into the acid chloride with phosphorus pentachloride (1·1 equiv.) in benzene (usually 10 ml.) and then treated, with stirring, with anhydrous stannic chloride (*ca.* 2·4 equiv.) in benzene (usually 2 ml.) in one portion. After 1 hr., ether was added and the whole poured on ice and hydrochloric acid. The organic layer was washed with 2N-hydrochloric acid, water, 2N-sodium hydroxide, and water, dried ($MgSO_4$), and chromatographed on alumina.

(1) β-(7-Methyl-1-naphthyl)propionyl chloride. The acid chloride (from 0·5 g.) of the acid was treated as described above. Isolation without chromatography afforded the perinaphthanone as crystals (0·36 g., 79%), m. p. 36—38·5°. The pale yellow colour was readily removed by passing its solution in light petroleum through alumina. On a larger scale, 2·8 g. gave 2·23 g. (87%), m. p. 34—38°, and 5·6 g. gave 4·48 g. (86·5%), m. p. 38—40°.

(2) β-(7-Ethyl-1-naphthyl)propionyl chloride. Obtained as above, the results were: 0·5 and 8·28 g. of acid gave 0·40 and 5·82—7·44 g., m. p. 60—62° and 60·5—62° (or 57—61·5°), respectively.

(3) β-(7-*iso*Propyl-1-naphthyl)propionyl chloride. Treated as above, 0·50 g. of acid gave 0·20 g. of pure product (43·6%).

(C) *With aluminium chloride on the acid chlorides in ethylene chloride or nitrobenzene.* The acid was converted into its acid chloride with thionyl chloride (2 ml. per g.) in ether (10 ml. per g.) containing pyridine (one drop). Excess of reagent and solvent were removed by evaporation with benzene, and the residue in pure ethylene chloride or nitrobenzene (20 ml. per g. of acid) was treated with aluminium chloride (1·1 equivs.) whilst being stirred at 15°. After 5 min. the solutions were allowed to reach room temperature during 1 hr. and poured on ice and hydrochloric acid. Ethylene chloride was removed by evaporation, nitrobenzene by steam-distillation. Acid washings of the products were pale yellow, but no pure organic material could be isolated from them. Final purification was usually carried out by chromatography on alumina. The results are in Table 3; they refer to 0·5 g. of acid.

TABLE 3.

| | Reaction in $(CH_2Cl)_2$ | | | Reaction in $Ph{\cdot}NO_2$ | | |
|---|---|---|---|---|---|---|
| Deriv. | State | M. p. | Yield (%) | State | M. p. | Yield (%) |
| 7-Me | Crude | 34—36° | 74·3 | — | — | — |
| | Chromatd. | 34—37 | 56·7 | Chromatd. | 38—39·5° | 57·6[c] |
| 7-Et | Crude | 58—60 | 74·8 | — | — | — |
| | Chromatd. | 59—61 | 82·5 | Cryst.[a] | 61—62 | 41·8 |
| 7-Pr$^i$ | Crude[b] | Oil | 96·4 | Crude[b] | Oil | 81·5 |

[a] From light petroleum (b. p. 40—60°). [b] No isomeric material found. [c] From 2·5 g. of acid.

(D) *With hydrogen fluoride.* The acid (1 g.) was treated with hydrogen fluoride (25 ml.), the latter being allowed to evaporate during 24 hr. The residue was washed with 2N-sodium hydroxide, and the product isolated with ether and purified by chromatography. The products were: Me, m. p. 35—39° (crude, 93·8% yield), 39—41° (pure, 44·8%); Et, m. p. 60—61·5° (crude, 92·8%), 61—62·5° (60·1%); Pr$^i$, oil (86·4% crude, 75·6% pure).

*Dehydrogenation of the Perinaphthanones.*—Details of the perinaphthenones (all yellow) are shown in Table 4. They were more strongly absorbed on alumina than the parent ketones and formed clear lemon-yellow bands easily eluted with benzene.

TABLE 4. *Perinaphthenones.*

| | | | Found (%) | | | Required (%) | |
|---|---|---|---|---|---|---|---|
| Deriv. | Form | M. p. | C | H | Formula | C | H |
| 9-Me ..... | Flakes | 91—93° | 86·1 | 5·0 | $C_{14}H_{10}O$ | 86·6 | 5·2 |
| 9-Et ..... | ,, | 65—66 | 85·6 | 5·6 | $C_{15}H_{12}O$ | 86·5 | 5·8 |
| 9-Pr$^i$ ..... | Oil [a] | — | 86·1 | 6·4 | $C_{16}H_{14}O$ | 86·5 | 6·4 |

[a] $n_D^{18}$ 1·6378. Decomposes when heated.

(1) 9-*Methylperinaphthanone.* (*a*) The ketone (0·30 g.) was heated with polyphosphoric acid (from 88% orthophosphoric acid, 2·5 g., and phosphoric oxide, 3·25 g.) for 1 hr., the mixture assuming a clear deep red colour. After working up in the usual way 9-methylperinaphthenone (0·040 g.), m. p. 84—88°, was obtained.

(*b*) The above method, with the addition of 25% palladised charcoal (0·3 g.), gave the unsaturated ketone (0·07 g.), m. p. 85—90°.

(*c*) The perinaphthanone (0·3 g.), 25% palladium–charcoal (0·3 g.), and glacial acetic acid (5 ml.) were refluxed together overnight. After cooling, water was added, the mixture filtered, the acid neutralised by the addition of 2N-sodium hydroxide, and the whole extracted with ether. Evaporation of the washed (water, saturated brine) and dried ($MgSO_4$) solution gave a yellow-brown solid. By absorption from benzene on alumina and elution with, first, 1 : 20 and then 1 : 10 ether–benzene the perinaphthenone (0·08 g.), m. p. 85—90°, was obtained.

(*d*) The ketone (0·3 g.), palladium–charcoal (0·3 g.), and trichloroacetic acid (10 g.) were refluxed together for 5 min. (evolution of hydrogen chloride). 9-Methylperinaphthenone (0·10 g., 33%), m. p. 85—90°, was isolated in the usual way.

(*e*) Bromine (theoretical amount) in carbon tetrachloride (2 ml.) was added dropwise to the ketone (0·3 g.) in hot carbon tetrachloride (15 ml.). An orange precipitate separated but disappeared on refluxing (5 min.). The solution was slowly evaporated, and the residual dark oil taken up in chloroform (5 ml.) and treated with anhydrous triethylamine (10 ml.). After 2 hr. the precipitated triethylamine hydrobromide was removed and washed with ether. Evaporation of the solution and washings left a dark solid which was thoroughly extracted with cold concentrated hydrochloric acid; the extract was diluted with water until turbidity appeared and then shaken with ether. The washed and dried ether solution was treated in the cold with a little charcoal and filtered. Evaporation and chromatography of the product from benzene on alumina furnished 9-methylperinaphthenone (0·11 g.).

(2) 9-*Ethylperinaphthanone.* Method 1(*d*), applied to the ethyl isomer, gave 30% of material, m. p. 61—64°. Method 1(*e*) gave 65% of material, m. p. 64—66°.

(3) 9-iso*Propylperinaphthanone.* (*a*) The ketone (0·51 g.), 25% palladium–charcoal (0·51 g.), and trichloroacetic acid (2 g.) were heated together at 100° overnight. Working up in the usual way furnished pure 9-*iso*propylperinaphthenone as a yellow acid-soluble oil (0·33 g.) which did not form a picrate.

(*b*) The perinaphthanone (0·65 g.) was treated with bromine and triethylamine as described above. The crude brownish-yellow oil (0·63 g.) was chromatographed on alumina (15 g. of active material, supplied by Savory and Moore Ltd.), and the product immediately rechromatographed in the same manner, elution being as rapid as possible. 9-*iso*Propylperinaphthenone was obtained as an analytically pure oil (0·56 g., 78%).

One of us (A. J. M. W.) is indebted to the Council of the University for a maintenance scholarship. We also thank the Chemical Society for a Research Grant and Imperial Chemical Industries Limited for financial aid.

WASHINGTON SINGER LABORATORIES,
PRINCE OF WALES ROAD, EXETER.

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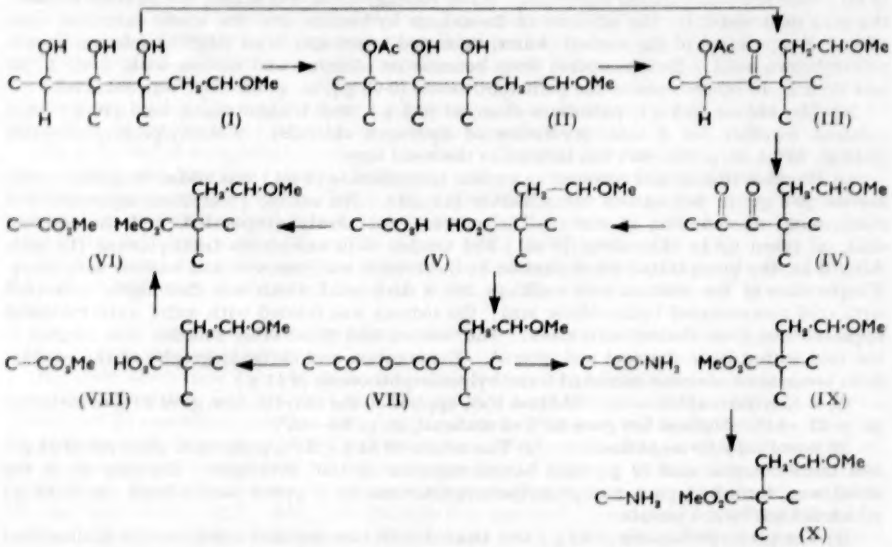
## 751. Aconitum *and* Delphinium *Alkaloids. Part III.* Some Rearrangements in the Delpheline and Lycoctonine Series. A Monobasic Dicarboxylic Acid.*

By R. C. Cookson and M. E. Trevett.

Acetyl chloride causes pinacolic dehydration of demethyleneoxodelpheline to an α-acetoxy-ketone that is converted *via* an α-diketone into a dicarboxylic acid. Although it undoubtedly contains two carboxyl groups, this acid titrates as a strong monobasic acid. On harsher treatment with acid further rearrangement occurs, giving an αβ-unsaturated ketone. Analogous rearrangements take place in the lycoctonine series.

Demethyleneoxodelpheline has been shown * to contain the group (I), which forms the secondary monoacetate (II) with acetic anhydride and pyridine. But treatment of the triol (I) with acetyl chloride caused dehydration as well as acetylation, with formation of a substance that formed no carbonyl derivatives under normal conditions but was recognised as a ketone by its characteristic absorption spectra, $\lambda_{max.}$ 293—294 mμ (ε 114) and $\nu_{max.}$ 1738 cm.$^{-1}$ (ketone and acetate superimposed, in Nujol). A choice amongst the various possible ways in which water might have been eliminated from the triol (I), either with or without rearrangement, was easily made when the pinacone acetate was found to be a secondary α-acetoxy-ketone.



Hydrolysis of the pinacone acetate gave an amorphous ketol, or mixture of ketols, that formed an isomeric acetate on re-acetylation, and was oxidised by chromic oxide in pyridine to a pale yellow, crystalline α-diketone. Thus the pinacone acetate must have the partial structure (III) and the α-diketone (IV).

The rather high frequencies (1758 and 1720 cm.$^{-1}$, in $CS_2$) of the C=O stretching vibrations of the α-diketone (IV) led us to consider that the diketone (IV) might be a *cyclo*pentanedione,[1] which would have required the three hydroxyl groups of the triol (I) to be attached

* Part II, *J.*, 1956, 3121.

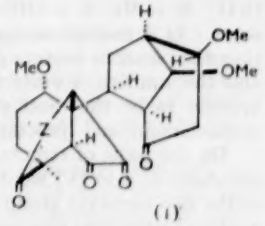
[1] Cookson and Trevett, *Chem. and Ind.*, 1954, 1391.

to the same *cyclo*pentane ring. But recent data[2] make it much more likely that it is a *cyclo*hexanedione formed from (I) by ring-expansion.

Unbridged *cyclo*hexanediones have their longest ultraviolet band[3,4] at about 350—380 mμ (in EtOH) and the two carbonyl-stretching bands,[3] which are not always resolved, between 1710 and 1730 cm.$^{-1}$ (in $CS_2$ or $CCl_4$). However, when the two carbonyl groups are kept coplanar by incorporation in a rigid, bridged ring, as in *bicyclo*[2 : 2 : 2]octane-2 : 3-dione, the ultraviolet maximum[2,5] is shifted to 478 mμ (strongest vibrational band in *cyclo*hexane solution: probably corresponding to about 460 mμ in EtOH) and the infrared bands[2,5] are shifted to 1730 and 1760 cm.$^{-1}$. In bridged *cyclo*pentanediones[2,6], such as *bicyclo*[2 : 2 : 1]heptane-2 : 3-dione,[2] the corresponding maxima are at about 470 mμ (EtOH) and at 1760 and 1770—1780 cm.$^{-1}$. The spectroscopic properties of the pinacone diketone (III) ($\lambda_{max.}$ 402 mμ; $\nu_{max.}$ 1720 and 1758 cm.$^{-1}$)* clearly point to a bridged *cyclo*hexanedione, although this evidence is not conclusive in view of the possibility of spectroscopic interaction between the functional groups. The α-diketone (IV) was inert to long boiling with acetic anhydride and sodium acetate, and did not show any other sign of enolising.

The carbonyl groups showed the hindrance usual in this series—for example, the diketone (IV) was unchanged by long treatment with *o*-phenylenediamine in boiling acetic acid—but when hydrogen peroxide was added to an alkaline solution of the diketone (IV) the colour rapidly faded, and a dicarboxylic acid (V) was formed. Presumably the small, almost linear, and strongly nucleophilic hydroperoxide anion can attack one of the carbonyl groups where larger reagents fail. The acid (V) gave the dimethyl ester (VI) with diazomethane and the cyclic anhydride (VII) with acetic anhydride. Although the acid (V) certainly contained two carbonyl groups, from its method of preparation and from the characteristic infrared spectra of its derivatives (VI) and especially (VII), it titrated in 50% ethanol as a remarkably strong *monobasic* acid (p$K'$ 3·75). Methoxide opened the anhydride (VII) to form an acid ester (VIII) in which the stronger carboxyl was esterified, allowing the weaker one to be titrated normally (p$K'$ 5·85). Diazomethane turned the acid ester (VIII) into the diester (VI), but the isomeric acid ester could not be obtained crystalline by partial hydrolysis of the latter.

If, as once seemed possible,[11] delpheline were a 1 : 2-amino-alcohol, the stronger carboxyl group in the acid (V) would have had the amide-nitrogen atom α to it, as in (A). The absence of such a group was demonstrated by opening the anhydride with ammonia to an amorphous amide-acid, converted by diazomethane into a crystalline amide-ester (IX). Treatment of the amide with hypobromite gave an amino-ester (X) that was

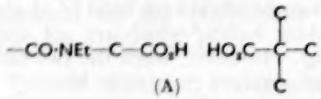


(I)

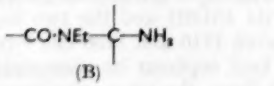
* The light absorption of the yellow *cyclo*hexanedione (IV) contrasts with that of the red *seco*-diketone[7] (i), a *cyclo*pentanedione ($\lambda_{max.}$ 490 mμ; $\nu_{max.}$ 1775 and 1755 cm.$^{-1}$), which absorbs at about 90 mμ longer wavelength in the ultraviolet and at substantially higher frequencies in the infrared. The long wavelength of the maximum of (i) compared with that of, say, camphorquinone (466 mμ) may be partly due to interaction with the adjacent amide group: cf. the orange 5 : 5-dihalogeno-3 : 3 : 4 : 4-tetramethyl*cyclo*pentane-1 : 2-dione,[8] the "bright raspberry-coloured" 2 : 2 : 5 : 5-tetramethyltetrahydro-3 : 4-dioxofuran,[9] and the "crimson-red" 5 : 5-dimethoxy-3 : 3 : 4 : 4-tetramethyl*cyclo*pentane-1 : 2-dione.[10] The last has $\lambda_{max.}$ 510 mμ.

[3] Alder, Schäfer, Esser, Krieger, and Reubke, *Annalen*, 1955, **593**, 23.
[2] Amongst others, Leonard and Mader, *J. Amer. Chem. Soc.*, 1950, **72**, 5388; Jones, Humphries, and Dobriner, *ibid.*, p. 956; Voser, Günthard, Heusser, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1952, **35**, 2065.
[4] Richter, Schindler, and Reichstein, *ibid.*, 1954, **37**, 76, and later papers in that series.
[5] See also Naffa and Ourisson, *Bull. Soc. chim. France*, 1954, 1115.
[6] Vaughan and Peters, *J. Org. Chem.*, 1953, **18**, 382; Eastman and Selover, *J. Amer. Chem. Soc.*, 1954, **76**, 4118.
[7] Cookson and Trevett, *J.*, 1956, 3121.
[8] Ingold and Shoppee, *J.*, 1928, 365.
[9] Dupont, Dulou, and Lefort, *Bull. Soc. chim. France*, 1949, 789; Korobitsyna, Yuryev, and Nefedova, *J. Gen. Chem. (U.S.S.R.)*, 1954, **24**, 188.
[10] Shoppee, *J.*, 1936, 269.
[11] Cookson and Trevett, *Chem. and Ind.*, 1954, 1324; cf. *J.*, 1956, 2689.

stable to boiling concentrated hydrochloric acid. Had the group (B) been present it would surely have been hydrolysed.




(A)




(B)

Acetyl chloride induced an analogous pinacolic dehydration of oxolycoctonine [12] and its derivatives to a pinacone, that on treatment with more strongly acidic reagents underwent a complex rearrangement with elimination of methanol and hydrolysis of a second methoxyl group to form an αβ-unsaturated ketone. Since Edwards and Marion [13] have independently discovered and investigated these two compounds, which they call " anhydrolycoctonam " and " lycoctamone," we include in the Experimental part of this paper only brief mention of some experiments that have not been duplicated. They could not, at that time, decide which carbon atom had migrated during the pinacol rearrangement, but the presence of the secondary hydroxyl group in demethyleneoxodelpheline (I) made the decision a simple one for us.

| | $\Delta[M]_D$ [a] | $\lambda_{max.}$ in mμ (ε) | $\nu_{max.}$ in cm.$^{-1}$ |
|---|---|---|---|
| Dehydroxymethyloxolycoctonine pinacone ..... | −250° [b] | 305 (83) [b] | 1730, 1637 [c] |
| Acetyldemethyleneoxodelpheline pinacone ..... | −140° [c] | 293—4 (114) [b] | 1738, 1636 [d] |
| Lycoctamone ..... | +800 [b] | 213 (12,300) [b] | 1675, 1620 [c] |
| | | 243 (10,500) | |
| | | 306 (310) | |
| Delphelamone ..... | +940° [c] | 215 (11,300) [b] | 1675, 1620 [c] |
| | | 243 (11,600) | |
| | | 314 (100) | |

[a] $[M]_D$ of derivative minus $[M]_D$ of corresponding unrearranged glycol. [b] Ethanol. [c] Chloroform. [d] Nujol.

In strongly acid media demethyleneoxodelpheline pinacone acetate (III) developed an ultraviolet maximum at 245 mμ (ε 10,000); treatment of oxodelpheline, *iso*oxodelpheline, or demethyleneoxodelpheline with, for example, boiling hydrochloric acid led to a crystalline αβ-unsaturated ketone which we call delphelamone, for it is, we shall show, the analogue of lycoctamone. The Table, summarising the optical properties of the products of rearrangement in the lycoctonine and delpheline series, brings out the very close resemblance between the two series.

Dehydration of oxolycoctonine (XI; R = Me, X = OH) must give the pinacone (XII; R = Me, X = OH): the stereochemistry is very favourable for such a rearrangement. If demethyleneoxodelpheline has the analogous structure [7] (XI; R = X = H), then the pinacone acetate (III) must have the complete structure (XII; R = Ac, X = H), and the isomeric acetate from hydrolysis and re-acetylation is probably (XIII), which appears to be the most stable of the four possible ketol acetates. The nature of the delphelamone and lycoctamone rearrangements will be discussed later.

On the basis of structure (XII; R = Ac, X = H) for the pinacone acetate (III), the dicarboxylic acid (V) would be (XIV).* The drawing (XV) illustrating the environment of the two carboxyl groups in this dicarboxylic acid shows how near they are held to one another by the rigid ring-system. The anion-acid will then be stabilised by an exceptionally strong internal hydrogen bond (XVI), while the dianion will be correspondingly destabilised by strong electrostatic repulsion and by hindrance to external hydrogen bonding and solvation.[14]

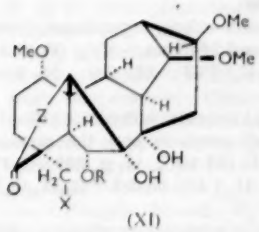
*cis*-Caronic acid [15] (3 : 3-dimethyl*cyclo*propane-1 : 2-*cis*-dicarboxylic acid) with p*K*

* Although one ring used for configurational reference is broken, to avoid confusion formula (XIV) is projected in the same way as the hexacyclic formulæ, so that the two carboxyl groups and the other carbon atoms of the former seven-membered ring and the six- and five-membered rings linearly condensed with it are taken as the reference system (see *J.*, 1956, 3124).

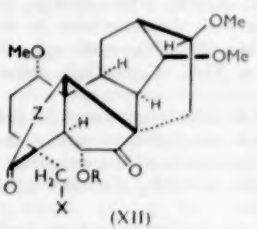
[12] Ref. 7, footnote, on p. 3124.
[13] Edwards and Marion, *Canad. J. Chem.*, 1952, **30**, 627; 1954, **32**, 708.

values in water of 2·34 and 8·31 seems to provide the closest analogy for the behaviour of the dicarboxylic acid * (XIV).

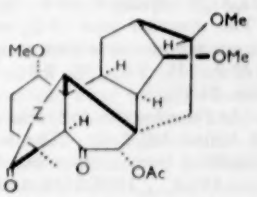
In (XI)—(XIV), Z = NEt



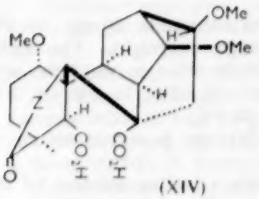
(XI)



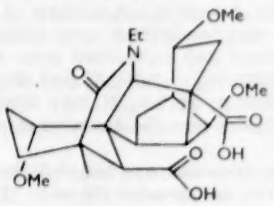
(XII)



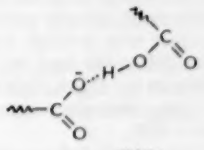
(XIII)



(XIV)



(XV)



(XVI)

## Experimental

Unless otherwise stated, rotations were measured in $CHCl_3$, ultraviolet spectra in EtOH, and apparent dissociation constants in ethanol–water (1 : 1 by vol.).

*Treatment of Demethyleneoxodelpheline with Acetyl Chloride.*—Demethyleneoxodelpheline (112 mg.) in acetyl chloride (5 ml.) was boiled for 6 hr. The product, isolated with chloroform (and kept away from alkali), crystallised from aqueous ethanol to give needles of the *pinacone acetate* (III) (50 mg.), m. p. 214—218°, $[\alpha]_D$ −15·5°, $\lambda_{max.}$ 293—294 mμ (ε 114), $\nu_{max.}$ 1738 (s) and 1636 cm.$^{-1}$ (Nujol) (Found : C, 65·5; H, 8·1; N, 2·8; OMe, 18·9. $C_{26}H_{37}O_7N$ requires C, 65·7; H, 7·9; N, 2·95; 3OMe, 19·5%). This acetate was changed by treatment with such alkaline reagents as alumina or potassium carbonate.

*Isomerisation of the Pinacone Acetate.*—The acetate (III) (186 mg.) in ethanol (6 ml.) and N-sodium hydroxide (10 ml.) was boiled for 2 hr. The oil (156 mg.), extracted with chloroform, was dissolved in acetyl chloride (5 ml.), left overnight, and then boiled for ½ hr. The resulting isomeric *acetate* (111 mg.) separated from aqueous ethanol in cube-like crystals, m. p. 217—219°, $[\alpha]_D$ −55°, $\lambda_{max.}$ 293 mμ (ε 45), $\nu_{max.}$ 1756, 1728, and 1654 cm.$^{-1}$ ($CS_2$) (Found : C, 65·9; H, 7·8; N, 3·1%).

*The α-Diketone.*—The oily ketol from hydrolysis of the pinacone acetate (III) (450 mg.), as above, was oxidised with chromic oxide (450 mg.) in pyridine (9 ml.) at room temperature overnight. Crystallisation of the product from aqueous ethanol gave pale yellow needles of the α-diketone (IV), m. p. 212—215°, $[\alpha]_D$ −72°, $\lambda_{max.}$ 402 mμ (ε 53), infl. 290 mμ (ε 150), $\nu_{max.}$ 1758, 1720, and 1658 ($CS_2$) (Found : C, 66·7; H, 7·7; N, 3·3. $C_{24}H_{33}O_6N$ requires C, 66·8; H, 7·7; N, 3·25%).

*The Monobasic Dicarboxylic Acid.*—Hydrogen peroxide (" 100-vol."; 15 ml.) was added to a

* Though it is obviously not a close analogue of the saturated dicarboxylic acid (XIV) we did titrate under the same conditions naphthalene-1 : 8-dicarboxylic acid, which has its two carboxyl groups close together. It titrated normally, showing an equivalent weight of half the molecular weight, and apparent p*K*'s of about 5·4 and 7·3.

[14] Bird and Cookson, *Chem. and Ind.*, 1955, 1479.

[15] Jones and Soper, *J.*, 1936, 133; see also Brown, McDaniel, and Häfliger in Braude and Nachod's " Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, 1955, p. 632; Cardwell, Dunitz, and Orgel, *J.*, 1953, 3740.

solution of the α-diketone (IV) (200 mg.) in 2% potassium hydroxide in methanol (35 ml.). An hour later the acidic product was separated and crystallised from ethyl acetate as a white, microcrystalline powder (160 mg.). This *dicarboxylic acid* (V) had m. p. 206° (decomp.), $[\alpha]_D$ −22°, $\nu_{max.}$ 1700 and 1645 ($CS_2$), or 1695 and 1646 cm.$^{-1}$ (Nujol), p*K′* 3·75 [Found : C, 61·8; H, 7·7; N, 3·3; OMe, 19·5%; equiv., 468 (phenolphthalein), 464 (electrometrically). $C_{34}H_{35}O_8N$ requires C, 61·9; H, 7·6; N, 3·0; 3OMe, 20·0%; *M*, 466].

The *dimethyl ester* (VI), made with diazomethane in methanol–ether, crystallised from aqueous acetone in prisms, m. p. 164—165°, $[\alpha]_D$ −36°, $\nu_{max.}$ 1728 and 1640 cm.$^{-1}$ ($CS_2$) (Found : C, 63·2; H, 7·9; N, 2·8; OMe, 31·6. $C_{36}H_{39}O_8N$ requires C, 63·3; H, 8·0; N, 2·8; 5OMe, 31·4%).

*The Dicarboxylic Anhydride.*—The dicarboxylic acid (V) (94 mg.) in acetic anhydride (10 ml.) was boiled for 6 hr. The solvent was removed under reduced pressure and the residue crystallised from acetone–ether as pyramids of the *anhydride* (VII) (83 mg.), m. p. 248—254°, $[\alpha]_D$ −45°, $\nu_{max.}$ 1800, 1758, and 1660 cm.$^{-1}$ ($CS_2$) (Found : C, 64·1; H, 7·45; N, 3·2. $C_{34}H_{33}O_7N$ requires C, 64·4; H, 7·4; N, 3·1%).

Hydrolysis of the anhydride with boiling 2N-sodium hydroxide gave a quantitative yield of the dicarboxylic acid (V), m. p. and mixed m. p. 201—203°.

*Methanolysis of the Dicarboxylic Anhydride.*—A solution of the anhydride (50 mg.) in 5% methanolic sodium methoxide (5 ml.) was left at room temperature overnight. The acidic product was isolated with chloroform and crystallised from acetone–ether to yield the *acid ester* (VIII) (38 mg.), m. p. 191—192°, $[\alpha]_D$ −30°, p*K′* 5·85 (Found : C, 62·4; H, 8·0; N, 3·1; OMe, 26·0. $C_{35}H_{37}O_8N$ requires C, 62·6; H, 7·8; N, 2·9; 4OMe, 25·7%).

Diazomethane turned the half-ester into the dimethyl ester (VI), m. p. and mixed m. p. 161—162°.

*The Methyl Ester-amide.*—Dry ammonia was bubbled through a boiling solution of the anhydride (50 mg.) in dioxan (30 ml.) and benzene (30 ml.). The acidic product, isolated with chloroform, did not crystallise, but treatment with diazomethane gave the *methyl ester-amide* (IX) which crystallised from ether in needles (30 mg.), m. p. 228—229°, $[\alpha]_D$ −5·5°, $\nu_{max.}$ 1728, 1670, and 1615 (primary amide), and 1630 cm.$^{-1}$ (lactam) ($CHCl_3$) (Found : C, 62·9; H, 8·1; N, 5·6. $C_{35}H_{38}O_7N_2$ requires C, 62·7; H, 8·0; N, 5·85%).

*The Methyl Ester-nor-amine.*—A solution of the methyl ester-amide (23 mg.), potassium hydroxide (14 mg.), and bromine (10 mg.) in dioxan (1 ml.) and water (5 ml.) was left at room temperature for 1 hr. (The colour faded in about 5 min.) After the solution had then been warmed to 50° for 30 min. the product was extracted with chloroform and crystallised from ether–benzene, to provide the *methyl ester-nor-amine* (X) (15 mg.), m. p. 184—187° (Found : C, 64·3; H, 8·7; N, 6·1. $C_{34}H_{38}O_6N_2$ requires C, 64·0; H, 8·5; N, 6·2%).

The amine (X) was recovered almost quantitatively from solution in concentrated hydrochloric acid at room temperature after 20 hr., in boiling concentrated hydrochloric–acetic acid (1 : 1) after 2 hr., and in boiling concentrated hydrochloric acid after 1 hr.

*Delphelamone.*—*iso*Oxodelpheline (22 mg.) in dioxan (1 ml.) and concentrated hydrochloric acid (2 ml.) was boiled for 10 min. Isolation with chloroform and crystallisation from ethyl acetate–*cyclo*hexane gave *delphelamone* (8 mg.), m. p. 247° (decomp.), $[\alpha]_D$ +281°, $\lambda_{max.}$ 215 (ε 11,300), 243 (ε 11,600), and 314 mμ (ε 100), $\nu_{max.}$ 1675 and 1620 cm.$^{-1}$ ($CHCl_3$) (Found : C, 66·75; H, 7·3; OMe, 7·45. $C_{33}H_{39}O_5N,\frac{1}{2}H_2O$ requires C, 66·65; H, 7·6; 1OMe, 7·8%).

*iso*Oxodelpheline (25 mg.), heated on a steam-bath for 1 hr. in formic acid (8 g.) and phosphoric acid (2 g.), gave a gum (25 mg.), having $\lambda_{max.}$ 245 mμ (ε 10,000), which on crystallisation yielded delphelamone, m. p. 238—240°, not depressed by the first sample. Treatment of oxodelpheline with hydrochloric acid or with phosphoric and formic acids also produced delphelamone.

*Acetylation of Lycoctonine.*—With acetic anhydride and pyridine or with acetic anhydride and a trace of sulphuric acid at room temperature lycoctonine formed a gummy monoacetate, which gave a crystalline *perchlorate*, m. p. 194—195° (decomp.) after recrystallisation from ethanol–ethyl acetate (Found : C, 53·1; H, 7·4. $C_{27}H_{44}O_{12}NCl$ requires C, 53·15; H, 7·3%).

Acetyl-lycoctonine perchlorate regenerates lycoctonine on alkaline hydrolysis. The crystalline acetyl derivative, characterised only by its acetyl value, made by long reaction of lycoctonine with acetyl chloride [16] may be a product of rearrangement : the published acetyl determinations agree better with values expected for an anhydro-acetate.

[16] Suginome and Ohno, *J. Fac. Science, Hokkaido Univ.*, 1950, Ser. III, **4**, 36.

*Acetyloxolycoctonine Pinacone.*—This substance, the anhydrolycoctonam acetate of Edwards and Marion,[13] was most conveniently made from methyl-lycoconitine hydriodide by conversion into the amorphous free base, oxidation with potassium permanganate in acetone to the amorphous oxo-derivative, and hydrolysis to oxolycoctonine, which without crystallisation was treated with acetyl chloride. Oxolycoctonine pinacone, prepared by hydrolysis of the acetate, agreed in its physical properties with those reported by Edwards and Marion,[13] and in $CS_2$ had $\nu_{max.}$ 1730 and 1630 cm.$^{-1}$.

*Lycoctamone.*—Oxolycoctonine pinacone (734 mg.) was shaken with a concentrated solution of zinc chloride[17] (14 ml. of a solution of 60 g. of $ZnCl_2$ in 20 ml. of 12% hydrochloric acid) at room temperature. Dissolution was complete after about 1 hr. and after 3·5 hr. the solution was diluted with water and extracted with chloroform, which was filtered through alumina to remove a trace of yellowish material that was difficult to get rid of by crystallisation. Large, cube-like crystals of lycoctamone separated from aqueous ethanol, and had m. p. 220—225°, $[\alpha]_D$ +257° (EtOH), $\lambda_{max.}$ 213 (ε 12,300), 243 (ε 10,500), and 306 mμ (ε 310), $\nu_{max.}$ 1660 and 1608 cm.$^{-1}$ (Nujol) (Found: C, 63·5, 63·55; H, 7·7, 7·6; OMe, 15·0; loss at 110° *in vacuo*, 4·1. Calc. for $C_{23}H_{31}O_6N,H_2O$: C, 63·4; H, 7·6; 2OMe, 14·3; $1H_2O$, 4·1%).

Oxolycoctonine pinacone (88 mg.), dissolved in 75% perchloric acid (1 ml.), was left at room temperature for 4·5 hr. The resulting gum crystallised under ether as lycoctamone (43 mg.), m. p. 210—215° (sintering at 208°, clear liquid at 219°) after recrystallisation from aqueous ethanol.

Lycoctamone acetate, made with acetic anhydride and pyridine and crystallised from aqueous ethanol, had m. p. 223—225°, $[\alpha]_D$ +215° (EtOH), $\nu_{max.}$ 1748, 1684, and 1640 ($CS_2$), or 1748, 1674, and 1622 cm.$^{-1}$ (Nujol) (Found: C, 65·4; H, 7·5; N, 3·25. Calc. for $C_{25}H_{33}O_7N$: C, 65·3; H, 7·2; N, 3·05%).

Lycoctamone (53 mg.) and 2 : 4-dinitrophenylhydrazine (39 mg.) in ethanol (2 ml.) and concentrated hydrochloric acid (4 drops) were boiled for 1 hr. The product, extracted with ethyl acetate, was adsorbed on to alumina from benzene. Benzene and ethyl acetate eluted negligible amounts of orange products, but chloroform removed 74 mg. that crystallised from aqueous methanol. The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate–*cyclo*hexane in bright red blades, m. p. 236—237°, $\lambda_{max.}$ 377 mμ (ε 28,100) in $CHCl_3$ (Found: C, 58·1; H, 6·0; N, 11·6. $C_{29}H_{35}O_9N_5$ requires C, 58·3; H, 5·9; N, 11·7%).

*Oxolycoctonine Pinacone Aldehyde.*—The pinacone (100 mg.) and chromic oxide (100 mg.) in pyridine (2 ml.) were left overnight. Extraction with chloroform and crystallisation from aqueous ethanol gave the corresponding *aldehyde* (60 mg.), m. p. 156—157°, $[\alpha]_D$ +54° (EtOH), $\lambda_{max.}$ 305 mμ (ε 117) (Found: C, 64·8; H, 7·5; N, 3·1. $C_{25}H_{35}O_7N$ requires C, 65·05; H, 7·6; N, 3·0%).

*Lycoctamone Aldehyde.*—Lycoctamone (150 mg.) and chromic oxide (150 mg.) in pyridine (3 ml.) were left for 2 hr. After crystallisation from ethyl acetate–*cyclo*hexane the resulting *aldehyde* (112 mg.) had m. p. 210—214°, $[\alpha]_D$ +282°, $\lambda_{max.}$ 213 (ε 12,250), 245 (ε 11,100), and 316 mμ (ε 57) (Found: C, 66·3; H, 7·2; N, 3·5. $C_{23}H_{29}O_6N$ requires C, 66·5; H, 7·0; N, 3·4%).

We are grateful to the Central Research Fund for a grant, to Glaxo Laboratories Ltd. for the infrared spectra, to Dr. B. J. Langdon for a generous supply of *Delphinium* shoots, and to Professor D. H. R. Barton, F.R.S., for his continued interest.

Birkbeck College, London, W.C.1. [*Received, May 23rd, 1956.*]

[17] Cf. Jacobs and Pelletier, *J. Amer. Chem. Soc.*, 1954, **76**, 161, and earlier papers.

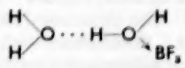
## 752. *Nuclear-resonance Spectra and the Structures of the Mono- and Di-hydrate of Boron Trifluoride.*

By P. T. Ford and R. E. Richards.

Proton and fluorine nuclear-resonance spectra are recorded for the mono- and the di-hydrate of boron trifluoride and for boron trifluoride dideuterate at 90° K. Different types of spectra are obtained when the samples are crystallised extremely slowly from those observed with rapidly cooled samples. In each case the results from the very slowly crystallised hydrates show that they crystallise in the un-ionised forms $BF_3,H_2O$ and $BF_3,2H_2O$; the spectra are not consistent with the fully ionised structures $[BF_3{\cdot}OH]^-H_3O^+$ or $BF_3,[BF_3{\cdot}OH]^-H_3O^+$. The spectra of the rapidly cooled samples are consistent with a partially ionised structure similar to that prevailing in the pure liquids.

Klinkenberg and Ketelaar [1] showed that the *X*-ray diffraction pattern of the boron trifluoride dihydrate at −60° closely resembles those of ammonium fluoroborate and ammonium perchlorate and concluded that the compound is fully ionised in the solid state and should be written $[BF_3{\cdot}OH]^-H_3O^+$. Sowa, Kroeger, and Nieuwland [2] suggested that the compound might be regarded as $[H_2F]^+[BF_2(OH)_2]^-$, but Greenwood and Martin's conductometric work [3] on the liquid showed that ionic dissociation gives the oxonium and the hydroxyfluoroborate ion. The degree of ionic dissociation at 25° was found to be about 10% for the monohydrate and 20% for the dihydrate.

The majority of boron trifluoride compounds are in the 1 : 1 molecular ratio. There are, however, about twenty cases known in which boron trifluoride combines with two donor molecules, and it has been pointed out by Meerwein and Pannwitz [4] that in all these cases the donor molecules are associated liquids. They suggest that the structure of the 1 : 2 complexes could be explained in terms of hydrogen bonding, *e.g.*,



Greenwood and Martin [3] regard these substances as oxonium compounds. The 1 : 2 complexes, when they occur, are always more stable than the corresponding 1 : 1 complexes, and the extra stabilisation is ascribed to the energy of solvation of the proton, *e.g.*, $H^+[BF_3{\cdot}OH]^-$, $H_3O^+[BF_3{\cdot}OH]^-$.

The ionic and non-ionic structures for these complexes have different groupings of protons and fluorine atoms, and nuclear-resonance experiments were undertaken to discover which of these arrangements occur in the crystalline materials.

### Experimental

The hydrates were prepared by passing the required amount of pure boron trifluoride (supplied by the Imperial Smelting Co.) into water. Both hydrates were purified by fractional crystallisation, at about 0°. The monohydrate is very readily supercooled, and it was therefore necessary to pre-freeze it at a very low temperature and then to warm it until only a small amount of crystalline material remained as a nucleus for the following crystallisations. Both pure hydrates formed large well-defined crystals. The monohydrate had m. p. 5·7°, $d^{25}$ 1·779, and the dihydrate m. p. 6·3°, $d^{25}$ 1·627. They cannot be distilled without risk of decomposition, so the pure liquids were poured into thin-walled Phoenix-glass ampoules and sealed off immediately.

Boron trifluoride dideuterate was prepared in a similar manner from 99·7% heavy water. A closed apparatus was used for the preparation and for the two fractional crystallisations;

[1] Klinkenberg and Ketelaar, *Rec. Trav. chim.*, 1935, **54**, 959.
[2] Sowa, Kroeger, and Nieuwland, *J. Amer. Chem. Soc.*, 1935, **57**, 454.
[3] Greenwood and Martin, *Quart. Rev.*, 1954, **8**, 1.
[4] Meerwein and Pannwitz, *J. prakt. Chem.*, 1934, **141**, 123.

the final product was sealed into an ampoule. The m. p. of the pure material was 11·2°. A sample of the gas released from the dideuterate by magnesium was analysed by a mass-spectrometer, and shown to contain 98·3% of deuterium.

Nuclear-magnetic-resonance measurements were made with the apparatus described by Richards and Smith [5] and Pratt and Richards.[6] A twin-T bridge method was used at frequencies near 12·2 Mc./sec. and derivatives of the absorption curves were obtained by automatic recording. The radiofrequency field was always reduced until no further change in the shape or width of the absorption line occurred; this ensures that the nuclear-resonance spectrum is not appreciably saturated.

*Other Compounds.*—Attempts were made to prepare pure samples of potassium hydroxyfluoroborate, $K^+[BF_3{\cdot}OH]^-$. The methods of Wamser [13] and of Ryss and Slutskaya [14] did not yield samples of satisfactory purity.

Paushkin and Topchiev [15] mention a compound of stoicheiometric formula $H_3O,HF,BF_3$, which might be $H_3O^+BF_4^-$. We were not able to obtain a compound of definite composition by passing boron trifluoride into an equimolar solution of hydrogen fluoride in water, although in one case a precipitate appeared when about 80% of the required $BF_3$ had been added which redissolved on increasing the amount of $BF_3$.

## Results

The absorption curves were obtained at 90° K and, for both the mono- and the di-hydrate, two types of spectra were observed according to the rate of cooling. If the samples were allowed

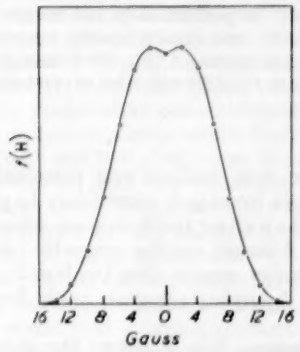



FIG. 1. *Proton resonance of* $BF_3,H_2O$ *at* 90° K *after very slow cooling. Circles are theoretical points for pairs of protons* 1·62 Å *apart, with a broadening function* $\beta^2 = 7{\cdot}2$ *gauss*$^2$.

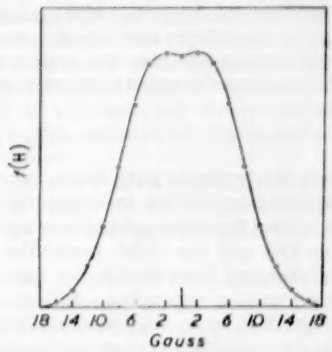



FIG. 2. *Proton resonance of* $BF_3,2H_2O$ *at* 90° K *after very slow cooling. Circles are theoretical points for pairs of protons* 1·54 Å *apart, with a broadening function* $\beta^2 = 9$ *gauss*$^2$.

to crystallise very slowly in the refrigerator for ≤24 hr., the proton-resonance spectra showed a doublet structure with a central minimum (see Figs. 1 and 2).

If the samples were very rapidly frozen by immersion in liquid air, the proton-resonance

| | Proton resonance | | Fluorine resonance | |
|---|---|---|---|---|
| Compound | Second moment (gauss$^2$) | Line width (gauss) | Second moment (gauss$^2$) | Line width (gauss) |
| $BF_3,H_2O$ : slowly cooled ..... | 27·2 ± 1·4 | 13·2 | 21·8 ± 1·2 | 11·5 |
| rapidly cooled ... | 26·1 ± 2·0 | 11·9 | 20·5 ± 0·8 | 7·6 |
| $BF_3,2H_2O$ : slowly cooled ... | 35·9 ± 2·1 | 15·6 | 25·0 ± 2·1 | 11·7 |
| rapidly cooled ... | 33·0 ± 1·8 | 14·3 | 20·3 ± 1·3 | 8·0 |
| $BF_3,2D_2O$ : slowly cooled ... | — | — | 18·1 ± 1·5 | 9·3 |

spectra were found never to have the doublet structure, but always had a central peak (see Figs. 3 and 4).

The second moments and line widths obtained at 90° K are given in the Table. The second

[5] Richards and Smith, *Trans. Faraday Soc.*, 1951, **47**, 1261.
[6] Pratt and Richards, *ibid.*, 1953, **49**, 744.

moments are not corrected for the effects of inhomogeneity of the magnetic field or for the finite amplitude of the modulation field. In these experiments these effects are 0·1 and 0·5 gauss[2] respectively and so to obtain the corrected values for the second moments 0·6 gauss[2] must be subtracted from the values given.

Intermediate line shapes could be obtained for the proton and fluorine resonances if the conditions of cooling were chosen appropriately, so the conditions used in these experiments were chosen as carefully as possible to favour one extreme or the other.

After slow cooling the sample tube always cracked when allowed to warm to room temperature, whereas this never happened with the samples which had been rapidly cooled. It was therefore possible to study the same sample first after having been rapidly cooled and then

FIG. 3. *Proton resonance of* $BF_3,H_2O$ *at 90° K after rapid cooling.*

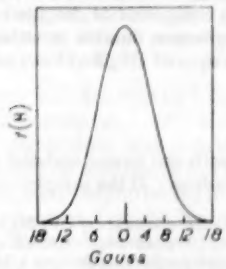
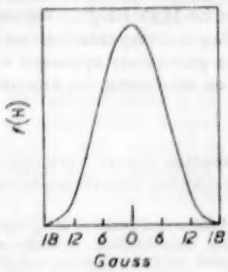



FIG. 4. *Proton resonance of* $BF_3,2H_2O$ *at 90° K after rapid cooling.*




after slow crystallisation, but the experiments could not be performed in the reverse order. The proton- and fluorine-resonance spectra of both slowly and rapidly cooled samples were measured without allowing the sample to warm. Experiments of this kind demonstrated that the differences observed in the spectra were due only to the different rates of crystallisation.

## DISCUSSION

When the hydrates were frozen very slowly the crystals obtained were presumably the most stable forms at the temperatures used, but rapid freezing is more likely to produce a solid having the same composition as the liquid at the melting point, or some composition between this and the stable crystalline form. The different nuclear magnetic resonance spectra obtained from slowly and rapidly cooled samples suggest that the liquid and the stable crystalline forms have different structures. A similar situation exists for liquid and crystalline nitric acid monohydrate.[5]

*The Monohydrate. Slow Cooling.—Proton resonance.* Fig. 1 shows the absorption curve obtained by taking the mean of five experimental curves. The central minimum is characteristic of a structure in which the protons are grouped in pairs. Very small traces of impurity in which the protons are not grouped in pairs will obscure this central minimum [7] and we believe that this must mean that the slowly cooled samples are pure materials. The circles in Fig. 1 were calculated for pairs of protons 1·62 Å apart, by use of a Gaussian broadening function [8] for which $\beta^2 = 7{\cdot}2$ gauss$^2$.

The close agreement between the experimental curve and the calculated points indicates strongly that the compound crystallises as the monohydrate, $BF_3,H_2O$. The H–H distance of 1·62 Å is quite consistent with a water molecule in which the O–H bond length and/or the HOH bond angle is very slightly increased from the values found in the gas. For example, if the HOH angle is 109° 30′, $d_{OH}$ is 0·99 Å, and if the HOH angle is 105°, $d_{OH}$ is 1·02 Å. The corresponding values [9] of the HOH angle and $d_{OH}$ for water in the gas phase are 105° 3′ and $0{\cdot}956_8$ Å.

Increase in the O–H bond length or the HOH angle by these amounts might be easily

[7] Deeley and Richards, *J.*, 1954, 3697.
[8] Pake, *J. Chem. Phys.*, 1948, **16**, 327.
[9] Herzberg, "Infrared and Raman Spectra," Van Nostrand, New York, 1945.

caused by the formation of strong hydrogen bonds or by co-ordination of the oxygen atom to the boron trifluoride molecule.

*Fluorine resonance.* The absorption spectrum of the slowly cooled material has a second moment of 21·8 ± 1·2 gauss². There is no satisfactory way to obtain the intermolecular broadening term, since the absorption line shows no structure and no *X*-ray measurements are available. However, this broadening can be roughly estimated at 7 gauss² because the intermolecular broadening found necessary for the proton-resonance spectrum was about 7 gauss². A large fraction of the intermolecular broadening is very likely to arise from H · · · F interactions in a lattice containing OH groups and F atoms.

If we estimate the intermolecular broadening of the fluorine resonance to be 7 gauss², this leaves about 15 gauss² as the intramolecular broadening of the $BF_3$ group. If this group were planar [10] with a B–F distance 1·30 Å, the intramolecular broadening would be 20·5 gauss², and if the FBF angle were tetrahedral with a B–F distance 1·43 Å (as in $BF_4^-$; Pendred and Richards [11]), then the intramolecular broadening would be 12·6 gauss². On the other hand, if the FBF angle were tetrahedral with a B–F distance 1·39 Å, as in $BF_3,NH_3$, $BF_3,NH_2{\cdot}CH_3$, and $BF_3,N(CH_3)_3$ (Hoard *et al.*[12]), the intramolecular broadening of the fluorine resonance would be 14·6 gauss².

The experimental value for the intramolecular term (with an assumed intermolecular broadening of about 7 gauss²) is about 15 gauss², and so the fluorine resonance can be interpreted plausibly in terms of a $BF_3$ molecule with a co-ordinated water molecule.

We therefore conclude that both the proton- and the fluorine-resonance spectrum of the slowly cooled samples of the monohydrate show them to consist of un-ionised $BF_3,H_2O$ molecules.

*The Monohydrate. Rapid Cooling.*—The proton resonance absorption curve (Fig. 3) shows no central minimum, and presumably this has been obscured by another curve which has a central maximum. This is readily understood if the rapidly cooled material is a mixture of $BF_3,H_2O$ (giving the pair structure with a central minimum) and $BF_3$ with the ions $[BF_3{\cdot}OH]^-$ and $[H_2O]^+$, both ions giving curves with central maxima. Unfortunately quantitative calculations are not possible in this case, but the second moment of the proton resonance would be expected to be slightly reduced by the contribution of the $[H_2O]^+$ and $[BF_3{\cdot}OH]^-$ ions, which is in fact observed.

The fluorine resonance would also be expected to have a smaller second moment if some ions were present because in the tetrahedral ion $[BF_3{\cdot}OH]^-$ the B–F distance is likely to be longer than in $BF_3$ [cf. $d_{B-F}$ in $BF_4^-$ = 1·43 Å (Pendred and Richards [11]); $d_{B-F}$ in $BF_3,NH_3$ = 1·39 Å (Hoard *et al.*[12])].

These results can be regarded as consistent with the presence of $BF_3,H_2O$ together with a small amount of the ionised form. They are not consistent with the fully ionised form, which would give a proton-resonance signal with a sharp central maximum due to the presence of the odd hydrogen atom in the $[BF_3{\cdot}OH]^-$ ion. It seems likely therefore that, on rapid cooling, the slightly ionised structure of the liquid is retained.

*The Dihydrate. Slow Cooling.*—Fig. 2 shows the average proton-resonance absorption curve obtained from twelve derivative curves. It shows a central minimum, characteristic of a lattice in which the protons occur in pairs. The circles in Fig. 2 are calculated points and correspond to an H–H distance of 1·54 Å with an additional gaussian broadening, for which $\beta^2$ = 9 gauss² (Pake [8]).

This result suggests strongly that the protons in the slowly cooled samples are again present in water molecules, so that the structure of the solid should be written $BF_3,2H_2O$. If we assume that the two water molecules have the same dimensions, then for an O–H distance of 0·96 Å (as in water vapour) the HOH angle would be about 107°. The results would also be consistent with the presence of two water molecules in which the H–H

[10] Levy and Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 2085.
[11] Pendred and Richards, *Trans. Faraday Soc.*, 1955, **51**, 468.
[12] Hoard, Geller, and Owen, *Acta Cryst.*, 1951, **4**, 405.
[13] Wamser, *J. Amer. Chem. Soc.*, 1948, **70**, 1209.
[14] Ryss and Slutskaya, *J. Gen. Chem. U.S.S.R.*, 1952, **22**, 41.
[15] Paushkin and Topchiev, *ibid.*, 1949, **19a**, 657.

distances were slightly different—one more than 1·54 Å, and one less. This H–H distance is consistent with the presence of water molecules in the lattice, although it is clear that at least one water molecule must have bond lengths and/or angles different, beyond experimental error, from those in $BF_3,H_2O$. This might occur if the dihydrate crystallised with one water molecule co-ordinated to the $BF_3$ (as in $BF_3,H_2O$) and other included in the lattice, probably with hydrogen bonds. These two water molecules might well have slightly different H–H distances. If the structure were $H_3O^+,BF_3{\cdot}OH^-$, then the absorption curve would have a strong central maximum, quite different from that observed.

The second moment of the fluorine resonance is 25 ± 2·2 gauss². This value is 3 gauss² higher than in the monohydrate, probably owing to increased intermolecular interaction from the protons of the second water molecule and also, possibly, to a slightly different FBF angle in the $BF_3$ group. The result is quite consistent, however, with the presence of $BF_3$ to which a water molecule is co-ordinated, and would be less consistent with a tetrahedral $[BF_3{\cdot}OH]^-$ ion, for which the B–F distance was 1·43 Å as in $BF_4^-$.

*The Dihydrate. Rapid Cooling.*—The proton-resonance absorption curve (Fig. 4) shows a broad central maximum, and the second moment is reduced from 36 to 33 gauss². This is consistent with the presence of some of the ionic species $[BF_3{\cdot}OH]^-$ and $[H_3O]^+$, both of which have proton arrangements which would contribute an absorption curve with a sharp central peak, thus obscuring the central dip due to the proton pairs.

The second moment of the fluorine resonance is decreased to 20 gauss² in the rapidly cooled sample. This may be attributed to the presence of the ionic form, of which the second moment of the fluorine resonance would be nearer 12·9 than 25 gauss². The lowering of the second moment is entirely consistent with a degree of ionisation of 20% (Greenwood and Martin [3]).

*The Dideuterate. Slow Cooling.*—The second moment of the fluorine resonance is 18 gauss². Since the deuterons have very small nuclear magnetic moments, most of this broadening must arise from interactions between fluorine atoms and between fluorine and boron atoms. The intermolecular broadening between fluorine atoms is probably quite small, with the two $D_2O$ molecules disposed in some way about the $BF_3$ group, so we estimate the intramolecular broadening for the $BF_3$ group to be about 15 gauss², similar to the value estimated in connexion with $BF_3,H_2O$. This would correspond to a B–F distance of about 1·38 Å and a tetrahedral FBF angle.

*Conclusion.*—The measurements described above show that in the stable crystalline state obtained by very slow cooling, the monohydrate and dihydrate of boron trifluoride have hydrogen atoms grouped only in pairs, and this must mean that their structures should be written as $BF_3,H_2O$ and $BF_3,2H_2O$.

If the samples are not frozen extremely slowly different results are obtained which can be interpreted in terms of the presence of small amounts of ionic species such as $[BF_3{\cdot}OH]^-$ and $[H_3O]^+$. This would be expected if the samples were frozen before the change from the partially ionised liquid to the stable un-ionised crystals could be completed.

The behaviour of these substances may be contrasted with that of nitric acid monohydrate (Richards and Smith [5]). The boron trifluoride hydrates and the nitric acid hydrate are both partially ionised in the liquid state. Whereas the former crystallises in the wholly un-ionised form, the latter crystallises in the completely ionised form. Very rapid freezing of the nitric acid monohydrate gave a solid having a composition corresponding to that of the liquid, just as has been found for the $BF_3$ hydrates.

We thank Dr. C. J. Danby for carrying out mass-spectrographic analyses, and the Department of Scientific and Industrial Research for a Maintenance Grant (to P. T. F.).

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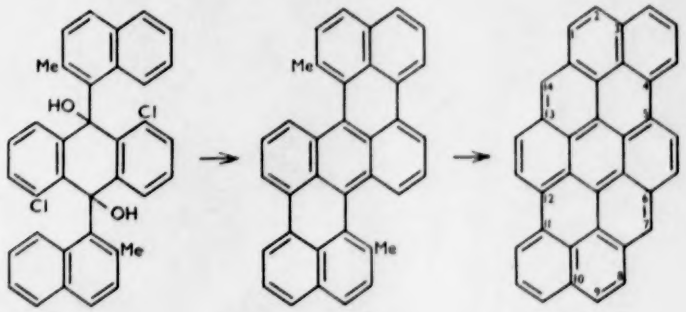
## 753. 3 : 4-5 : 6-10 : 11-12 : 13-*Tetrabenzoperopyrene.*

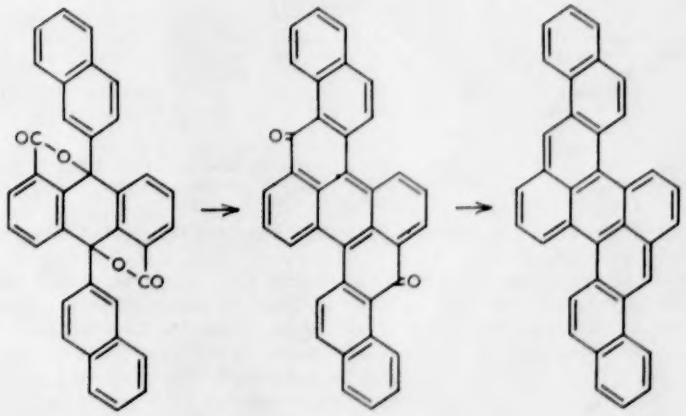
By E. Clar and W. Kelly.

Tetrabenzoperopyrene (III) was synthesised starting from 1 : 5-dichloroanthraquinone and 2-methyl-1-naphthylmagnesium bromide. The dimethyl compound (II) was obtained as an intermediate. The hydrocarbon (III) is different from Scholl and Meyer's dinaphthocoronene which is probably a dinaphthoperylene. It is also not identical with a hydrocarbon, claimed to be tetrabenzoperopyrene, obtained from the hydrogenation of coal.

1 : 5-Dichloroanthraquinone reacts with 2-methyl-1-naphthylmagnesium bromide to give the diol (I) which was reduced by hydriodic acid to the corresponding anthracene. When the latter was heated for a short time with potassium hydroxide in quinoline,




(I) (II) (III)




(IV) (V) (VI)

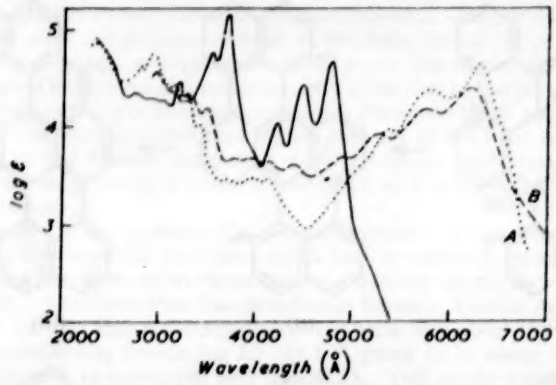
preferably under nitrogen, the blue 7′ : 7″-dimethyl-1 : 9-5 : 10-di*peri*naphthyleneanthracene (II) was obtained. The hydrocarbon (II) has properties similar to those of the unmethylated hydrocarbon.[1] The absorption spectra of the two hydrocarbons are given in the Figure. The relatively small differences between the two spectra were to be expected from the overcrowding by the methyl groups in the derivative (II). This causes

[1] Clar, Kelly, and Wright, *J.*, 1954, 1108.

a violet-shift of the long-wavelength bands and a flattening of the whole curve. This characteristic has also been observed in other cases.[2]

When 1 : 5-dichloro-9 : 10-di-(2-methyl-1-naphthyl)anthracene was heated for a longer time with potassium hydroxide and quinoline and in the presence of oxygen a further double cyclisation, involving the methyl groups, took place with the formation of the orange tetrabenzoperopyrene (III), the absorption spectrum of which, compared with that of the dimethyl compound (II), shows a large violet-shift. This compares strikingly with the strong red-shift which is observed when the two CH groups in the positions 7 and 14 were replaced by oxido-groups.[3]

The tetrabenzoperopyrene is not identical with the dinaphthocorene to which Scholl and Meyer[4] assign the same formula. The above synthesis does not allow any other course than the formation of (III). Scholl, Meyer, and Winkler,[5] however, assumed that the reaction of anthraquinone-1 : 5-dicarboxylic acid *pseudo*-chloride with naphthalene and aluminium chloride in nitrobenzene would give the di-α-naphthyl-dilactone. They




*A*, *Absorption spectrum of* 1 : 9-5 : 10-*diperinaphthyleneanthracene*. *Max.* (Å; log ε *in parentheses*) : 6300 (4·64), 5790 (4·40), 5360 (3·96); 4120 (3·47), 3920 (3·47), 3720 (3·47); 3420 (4·02), 3280 (4·36), 3120 (4·44), 2920 (4·76) *in benzene*; 2360 (4·88) *in alcohol*.

*B*, *Absorption spectrum of* 7' : 7''-*dimethyl*-1 : 9-5 : 10-*diperinaphthyleneanthracene* (II). *Max.* : 6210 (4·40), 5780 (4·19), 5250 (3·92); 4390 (3·60), 3980 (3·66), 3780 (3·67); 3510 (4·18), 3320 (4·27), 3150 (4·34); 2960 (4·56), *in benzene*.

*C*. *Absorption spectrum of* 3 : 4-5 : 6-10 : 11-12 : 13-*tetrabensoperopyrene* (III). *Max.* : 4780 (4·68), 4490 (4·44), 4220 (4·04); 3715 (5·14), 3540 (4·76) *in* 1-*methylnaphthalene*; 3200 (4·48), 3020 (4·32), 2750 (4·36) *in dioxan*.

failed to prove this and it is probable that the compound which they isolated was the di-β-naphthyl derivative (IV).

Cyclisation of the lactone (IV) would yield only the dinaphthoperylenequinone (V), whereas the α-derivative would give, first, an isomeric dinaphthoperylenequinone and then dinaphthocoronenequinone. Scholl and Meyer claimed to have obtained the latter two quinones but reported that there was apparently no difference in their properties. It is suggested that they were actually the same compound, the dinaphthoperylenequinone (V). After reduction and dehydrogenation this could yield the dinaphthoperylene (VI). The reported properties of Scholl and Meyer's hydrocarbon are compatible with the structure (VI).

When coronene is prepared by hydrogenation of coal a more highly condensed hydrocarbon is obtained as a by-product which Fromherz, Thaler, and Wolf[6] consider to be

[2] Brockmann and Randebrock, *Chem. Ber.*, 1951, **84**, 533.
[3] Clar, Kelly, Stewart, and Wright, *J.*, 1956, 2652.
[4] Scholl and Meyer, *Ber.*, 1934, **67**, 1229.
[5] Scholl, Meyer, and Winkler, *Annalen*, 1932, **494**, 220.
[6] Fromherz, Thaler, and Wolf, *Z. Elektrochem.*, 1943, **49**, 387.

identical with Scholl and Meyer's hydrocarbon. They do not report a direct comparison of the two hydrocarbons. The absorption spectrum of the hydrocarbon of Fromherz *et al.* is quite different from the spectrum of our compound (III). Therefore, their hydrocarbon must have some other structure.

## Experimental

M. p.s were taken in evacuated capillaries. Microanalyses are by Mr. J. M. L. Cameron and Miss M. W. Christie.

1 : 5-*Dichloro*-9 : 10-*dihydro*-9 : 10-*di*-(2-*methyl*-1-*naphthyl*)*anthracene*-9 : 10-*diol* (I).—A suspension of finely powdered 1 : 5-dichloroanthraquinone (35 g.) in benzene (300 ml.) was added with stirring during 30 min. to 2-methyl-1-naphthylmagnesium bromide prepared from 1-bromo-2-methylnaphthalene (110 g.) and magnesium (12 g.) in ether (250 ml.). The temperature was allowed to rise during the addition. 250 ml. of solvent were distilled from the mixture which was then heated under reflux on a water-bath for 2 hr. with continuous stirring. The thick suspension was decomposed by pouring it into dilute acetic acid containing ice. Benzene and some methylnaphthalene were removed by steam-distillation. The product was triturated with ether (1 l.) and digested twice with a large excess of alkaline sodium dithionite solution, a light fawn powder (26 g.) being obtained. Crystallisation from 1 : 2 : 4-trichlorobenzene gave the colourless *diol* (I), m. p. 329—330° (decomp.) (Found : C, 77·1; H, 4·8; Cl, 13·1. $C_{36}H_{26}O_2Cl_2$ requires C, 77·0; H, 4·7; Cl, 12·6%). It dissolved to give a green colour in concentrated sulphuric acid.

1 : 5-*Dichloro*-9 : 10-*di*-(2-*methyl*-1-*naphthyl*)*anthracene*.—A suspension of the diol (I) (10 g.) in acetic acid (70 ml.) and 55% hydriodic acid (7 ml.) was heated under reflux for 1 hr. The product was sublimed in a vacuum and the yellow sublimate (7 g.) was crystallised from 1 : 2 : 4-trichlorobenzene to give pale yellow 1 : 5-*dichloro*-9 : 10-*di*-(2-*methyl*-1-*naphthyl*)-*anthracene*, m. p. 359—360° (Found : C, 82·25; H, 5·1; Cl, 13·0. $C_{36}H_{24}Cl_2$ requires C, 82·0; H, 4·6; Cl, 13·4%).

7′ : 7″-*Dimethyl*-1 : 9-5 : 10-*diperinaphthyleneanthracene* (*Ring Index No.* 3943 : 9 : 18-*Dimethyltetrabenzo*[de, hi, op, st]*pentacene*) (II).—A mixture of the reduced 1 : 5-dichloro-compound (2 g.), potassium hydroxide (5 g.), and quinoline (11 ml.) was heated under reflux for 23 min. in an atmosphere of nitrogen. The reddish-violet solution was poured into dilute hydrochloric acid and the dark blue precipitate was extracted with benzene (150 ml.). The extract was chromatographed on alumina, the column being protected from the light. Elution, under pressure, with benzene–light petroleum (b. p. 40—60°) (1 : 2) gave an orange solution with a green fluorescence of the monocyclised compound, the benzoperylene derivative. A second blue band was eluted with benzene and yielded deep blue crystals, m. p. 382—383°, of the *hydrocarbon* (II) (Found : C, 94·95; H, 4·8. $C_{36}H_{22}$ requires C, 95·1; H, 4·9%). The blue solution, which has a red fluorescence, was photo-oxidised quickly. The compound dissolved in concentrated sulphuric acid to give a reddish-brown solution.

3 : 4-5 : 6-10 : 11-12 : 13-*Tetrabenzoperopyrene* (III).—A mixture of the reduced dichloro-compound (5 g.), potassium hydroxide (25 g.), and quinoline (30 ml.) was heated under reflux for 90 min. The quinoline solution was poured into dilute hydrochloric acid, and the dark precipitate was extracted (Soxhlet) with xylene until the extract was almost colourless. The red xylene solution yielded a small quantity of a very soluble red mixture of compounds which were not identified. The residue from the xylene extraction was then extracted with 1 : 2 : 4-trichlorobenzene to give a low yield of orange-brown leaflets. They were dissolved in trichlorobenzene and chromatographed on alumina at 140° with trichlorobenzene as eluant. The yellow eluate had a strong green fluorescence and yielded orange feathery needles, m. p. 487—488°, of *tetrabenzoperopyrene* (Found : C, 96·3; H, 3·9. $C_{36}H_{16}$ requires C, 96·4; H, 3·6%). The compound dissolved in hot concentrated sulphuric acid to give a green solution.

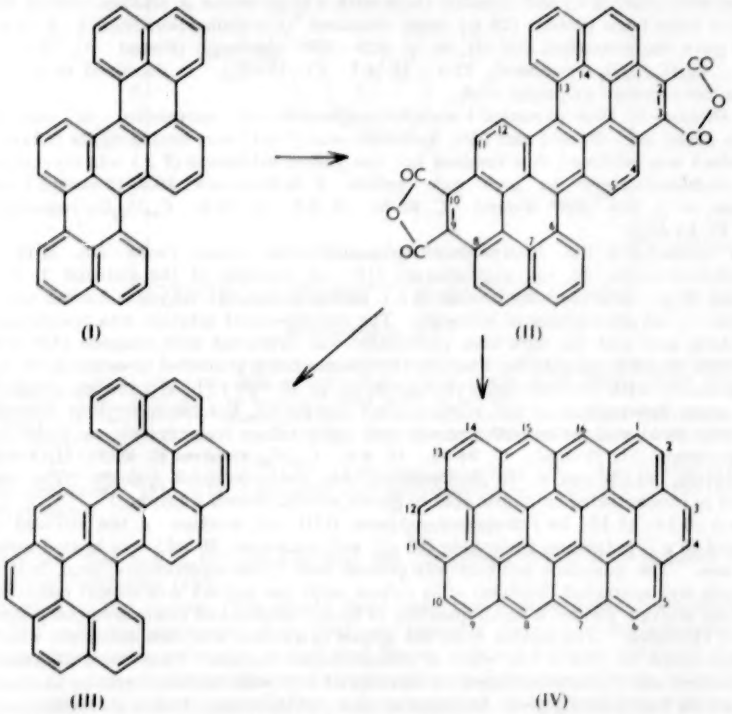
The University, Glasgow. [*Received, March 19th, 1956.*]

## 754. *Circumanthracene and Dinaphtho*(7′ : 1′-1 : 13)(1″ : 7″-6 : 8)-*peropyrene.*

By E. Clar, W. Kelly, J. Monteath Robertson, and M. G. Rossmann.

Di*peri*naphthyleneanthracene (I) was condensed doubly with maleic anhydride with the formation of the compound (II), which with copper powder and quinoline gave the hydrocarbon (III). Decarboxylation with soda-lime yielded the same hydrocarbon (III) and the more condensed product (IV), whose structure was proved by *X*-ray examination.

When di*peri*naphthyleneanthracene * (I) is melted with maleic anhydride one molecule of the latter is added endocyclically in the central anthracene complex.[1] This adduct dissociates into its components when heated above 200°. However, if the hydrocarbon (I) is boiled with maleic anhydride in presence of chloranil as dehydrogenating agent, two molecules are fused to it, with the formation of the tetracarboxylic dianhydride (II) in the



(I) (II) (III) (IV)

same way as perylene reacts with one molecule of maleic anhydride.[2] The decarboxylation of this adduct with copper powder in boiling quinoline gives the orange-red dinaphthoperopyrene (III), whose absorption spectrum is reproduced in the Figure together with the spectrum of the starting material (I). The additional two benzene rings cause a strong violet-shift of the long-wavelength bands which is about twice the shift found in passage from perylene

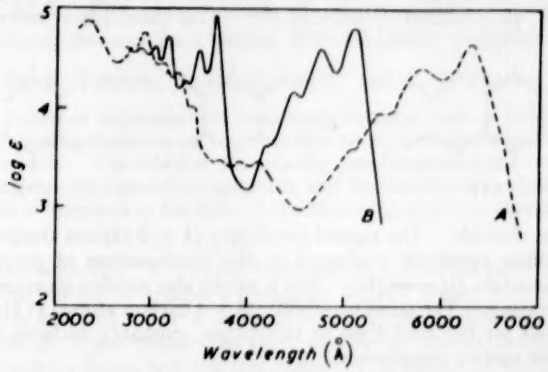
* The crystal structure of di*peri*naphthyleneanthracene has now been determined by *X*-ray analysis. This work will be published shortly.

[1] Clar, Kelly, and Wright, *J.*, 1954, 1108.
[2] Clar, *Ber.*, 1932, **65**, 846.

to 1 : 12-benzoperylene. Treatment of the adduct with soda-lime at 400°, however, yields, besides the dinaphthoperopyrene (III), a higher-melting, less volatile hydrocarbon which sublimes in dark needles and gives a red solution in 1-methylnaphthalene.

The properties of this new hydrocarbon indicated that it might be formed by " controlled graphitisation " and might have the structure (IV), and this structure was proved by *X*-ray investigation which revealed the presence of the carbon atoms in the positions 8 and 16. This new hydrocarbon which is the third member of a series beginning with coronene and ovalene might be called " circumanthracene," because of the central anthracene complex which is completely surrounded by condensed benzene rings.

Measurement of the grey-black prismatic needles with copper $K\alpha$ radiation ($\lambda$ 1·54 Å) showed that they are monoclinic with $a = 23{\cdot}77 \pm 0{\cdot}01$, $b = 4{\cdot}59 \pm 0{\cdot}03$, $c = 9{\cdot}98 \pm 0{\cdot}01$ Å, $\beta = 99° 54' \pm 30'$. The (*h*0*l*) spectra are absent when *h* is odd, and (0*k*0) when *k* is odd. The space group is therefore uniquely determined as $P2_1/a$ ($C_{2h}^5$). The




*A*, *Absorption spectrum of* 1 : 9-5 : 10-*diperinaphthyleneanthracene* (I). *Max.* (Å; log ε *in parentheses*) : 6300 (4·64), 5790 (4·40), 5360 (3·96); 4120 (3·47), 3920 (3·47), 3720 (3·47); 3420 (4·02), 3280 (4·36), 3120 (4·44), 2920 (4·76) *in benzene*; 2360 (4·88) *in alcohol*.

*B*, *Absorption spectrum of dinaphtho*(7′ : 1′-1 : 13)(1″ : 7″-6 : 8)*peropyrene* (III). *Max.*: 5100 (4·80), 4760 (4·59), 4470 (4·16); 3670 (4·92), 3490 (4·58), 3340 (4·26); 3170 (4·72), 3040 (4·61), 2900 (4·59) *in benzene*.

volume of the unit cell is $1075 \pm 6$ Å$^3$. The density of the crystals, measured by flotation in potassium iodide solution, at 20° is $1{\cdot}52 \pm 0{\cdot}01$.

The space group $P2_1/a$ requires four asymmetric molecules or two centrosymmetric molecules per unit cell. If we assume two molecules, the above data give *M* $492 \pm 5$ (Calc. for $C_{40}H_{16}$ : *M*, 496·5. Calc. for $C_{35}H_{18}$ : *M*, 474·5).

The molecular weight is thus established with considerable accuracy, but much more detailed evidence regarding the structure of the molecule can be obtained by comparing the crystal data with those for coronene and ovalene (see Table). The *b* and *c* axes remain

*Crystal data.*

| | *a* (Å) | *b* (Å) | *c* (Å) | $\beta$ | Space group | *Z* | *d* | *M* |
|---|---|---|---|---|---|---|---|---|
| Coronene, $C_{24}H_{12}$ ..... | 16·1 | 4·70 | 10·2 | 110·8° | $P2_1/a$ | 2 | 1·38 | 300 |
| Ovalene, $C_{32}H_{14}$ ..... | 19·5 | 4·70 | 10·1 | 105·0 | $P2_1/a$ | 2 | 1·49 | 398 |
| Circumanthracene, $C_{40}H_{16}$ | 23·8 | 4·59 | 10·0 | 99·9 | $P2_1/a$ | 2 | 1·52 | 496 |

very constant for the three crystals, but there is a steady increase in *a* and decrease in $\beta$ as we pass from coronene to circumanthracene. This is strong evidence that all these crystals are of the same structural type, a conclusion which is confirmed in detail by a study of the *X*-ray spectra.

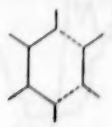
By setting up a trial structure based on the analogy with coronene and ovalene it was found that most of the (*h*0*l*) structure factors could be explained. A Fourier synthesis

based on this trial structure yielded a very clear electron-density projection of the molecule, which showed all the carbon atoms in the positions expected from structure (IV). Further refinement is proceeding, but is difficult because of a rapid decrease in the intensities of the high-order reflections, which appears to be due to an unusually high temperature factor. At the present stage of refinement, however, the discrepancy between calculated and observed structure factors has been reduced to about 19%. At this point there can now be no reasonable doubt that the structural formula is correct.

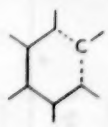
The origin of the carbon atoms in the positions 8 and 16 is not yet clear. They might come from the carbonyl groups or from the breakdown of another part of the molecule of the adduct (II) during the treatment with soda lime at 400°. (The problem is being studied in this Department, by means of the $^{14}C$ isotope.) The gap-filling in formula (III) is an example of the least well-known mechanism of ring formation in the course of graphitisation and building up a condensed ring system.

The best-known mechanism is the frontal condensation of 3 + 3 carbon atoms of two polycyclic systems, as indicated in diagram (V). This takes place under the influence of

(V)



(VI)




(VII)

heat or aluminium chloride. The second possibility (4 + 2 carbon atoms) is given in (VI). It constitutes a diene synthesis analogous to the condensation of perylene with maleic anhydride or the reaction (I) ⟶ (II). But it might also involve an aromatic double bond at a higher temperature. The third possibility (5 + 1 carbon atoms) (VII), which seems to have been reported for the first time in this paper, probably includes the formation of radicals or bivalent carbon compounds.

## Experimental

M. p.s were taken in evacuated capillaries. Microanalyses are by Mr. J. M. L. Cameron and Miss M. W. Christie.

*Dinaphtho*(7′ : 1′-1 : 13)(1″ : 7″-6 : 8)*peropyrene*-2 : 3 : 9 : 10-*tetracarboxylic Dianhydride* (II).—Di*peri*naphthyleneanthracene (I) (2 g.) and maleic anhydride (25 g.) were heated under reflux for 15 min. Chloranil (7 g.) was added and the reaction continued for 2½ hr. The colour changed from violet-red to reddish-brown and a solid was precipitated. Boiling xylene was added and the precipitate filtered off hot and washed with hot xylene. The dark purplish precipitate of the dianhydride (II) could not be successfully crystallised from any solvent. It was dissolved in ethanolic potassium hydroxide, and the solution diluted with water and acidified to give a dark purplish-red precipitate of the *tetracarboxylic acid* (Found : C, 76·4; H, 3·1. $C_{42}H_{18}O_8$ requires C, 77·5; H, 2·8%). The acid dissolved in warm concentrated sulphuric acid to a greenish-blue solution.

*Dinaphtho*(7′ : 1′-1 : 13)(1″ : 7″-6 : 8)*peropyrene* (III) *and Circumanthracene* (IV).—(a) *Decarboxylation with soda-lime.* The dianhydride (2·4 g.) and soda-lime (20 g.) were ground together to a smooth paste with a little alcohol. The mixture was heated at atmospheric pressure in a sublimation tube to remove moisture, and the pressure was slowly reduced. The mixture was heated at about 400°/1 mm. until no further material sublimed (about 12 hr.). The sublimate was extracted several times with boiling xylene. The crystals which separated from the combined extracts were filtered off and the xylene filtrate was concentrated and chromatographed on alumina with benzene as eluant. The orange-red eluate had a green fluorescence and yielded fine orange-red needles (0·1 g.), m. p. 338—339°, of *dinaphthoperopyrene* (III) (Found : C, 96·3; H, 3·8. $C_{38}H_{18}$ requires C, 96·2; H, 3·8%). It dissolved in warm concentrated sulphuric acid to a magenta solution.

The residue from the xylene extraction was crystallised from 1 : 2 : 4-trichlorobenzene, and the crystals were combined with those from the xylene extraction and chromatographed on alumina with trichlorobenzene as eluant. The first, reddish band yielded a small quantity of

dinaphthoperopyrene. A second, reddish-purple band on elution gave a deep red solution from which were obtained long black needles of *circumanthracene* (IV) which sinter at 480° but do not melt clearly at higher temperatures (Found: C, 96·3, 96·5; H, 3·45, 3·6. $C_{40}H_{18}$ requires C, 96·75; H, 3·25%). It dissolved with an orange colour in concentrated sulphuric acid.

(b) *Decarboxylation with copper powder.* A small quantity of the dianhydride (II) was heated with some copper powder in quinoline for 2 hr. The quinoline solution was filtered into dilute hydrochloric acid, and the precipitate sublimed in a vacuum. The dark reddish sublimate contained no trace of circumanthracene and on purification was identical with the dinaphthoperopyrene obtained as above.

THE UNIVERSITY, GLASGOW. [*Received, March 19th*, 1956.]

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## 755. *Interaction of Lewis Acids with Aromatic Hydrocarbons and Bases. Part XVII.* The Association of Hexamethylbenzene with Substituted* p*-Benzoquinones in Carbon Tetrachloride Solution.*

By R. FOSTER, D. LL. HAMMICK, and P. J. PLACITO.

The degree of interaction of hexamethylbenzene with a series of substituted *p*-benzoquinones in carbon tetrachloride solution has been determined colorimetrically. The relation between the free energies of the interaction, evaluated from the association constants, and the energies of excitation of the complexes is discussed in the light of Mulliken's [1] concept for charge-transfer complexes.

IN a previous communication [2] a relation between the ionisation potential of an electron donor and the free energy of complex formation by the donor with electron-accepting molecules was demonstrated. For a series of methylbenzenes interacting with chloranil in *cyclo*hexane solution, it was found that there is a linear relation between the ionisation potential of the electron donor and the free energy of formation of the complex, and also between the ionisation potential of the electron donor and the energy of excitation of the complex as measured by the wave-number of the maximum of the charge-transfer band. In the present communication, the effect of varying the acceptor component of the complex has been studied. Hexamethylbenzene was chosen as the donor since it has already been shown to be a powerful Lewis base in this type of interaction.[2,3]

The degree of association of hexamethylbenzene with a series of substituted *p*-benzoquinones has been determined spectroscopically. It has been assumed that the complexes are all of the charge-transfer type described by Mulliken,[1] in which the concentrations of the complexes may be determined by the intensities of the absorption bands which are characteristic of the complexes themselves. The algebraic method of evaluating the association constants used is that described by McConnell and his co-workers,[4] in which allowance is made for the absorption due to uncomplexed acceptor molecules. The method of evaluation also gives values of the molecular extinction coefficients of the complexes at the wavelength at which the determinations are made.

### EXPERIMENTAL

*Preparation and Purification of Materials.—Carbon tetrachloride.* The "AnalaR" reagent, purified by the method of Gunther, von der Horst, and Cronheim,[5] had $n_D^{19}$ 1·4604—1·4606, b. p. 76·0—76·5°/756 mm.; Gunther *et al.* give $n_D^{19.5}$ 1·46040, b. p. 76·71°/760 mm.

* Part XVI, *J.*, 1956, 555.

[1] (*a*) Mulliken, *J. Amer. Chem. Soc.*, 1950, **72**, 605; (*b*) *ibid.*, 1952, **74**, 811; (*c*) *J. Phys. Chem.*, 1952, **56**, 801.
[2] Foster, Hammick, and Parsons, *J.*, 1956, 555.
[3] Briegleb and Czekalla, *Z. Electrochem.*, 1954, **58**, 249.
[4] (*a*) Laudauer and McConnell, *J. Amer. Chem. Soc.*, 1952, **74**, 1221; (*b*) Lawrey and McConnell, *ibid.*, p. 6175.
[5] Gunther, von der Horst, and Cronheim, *Z. Electrochem.*, 1928, **34**, 616.

*Hexamethylbenzene.* Sublimed twice, and then recrystallised twice from ethanol, this had m. p. 162·5—163·5°. Briegleb and Czekalla [3] give m. p. 164·5°.

*Chloranil.* Recrystallised four times from benzene, this formed yellow plates, m. p. (sealed tube) 289° (Graebe [6] gives m. p. 290°).

p-*Benzoquinone.* Recrystallised twice from chloroform, the quinone formed orange prisms, m. p. 112·7°. Another sample was sublimed three times, as yellow needles, m. p. 113·5°. Hassel and Naeshagen [7] give m. p. 116·5°; Hammick Hampson, and Jenkins [8] give m. p. 112·8—113·6°; Briegleb and Czekalla [3] give m. p. 113·5°.

*Toluquinone.* Two recrystallisations from ethanol, rapid drying and storage *in vacuo* gave bronze plates and needles, m. p. 67·5°; Nietzski [9] gives m. p. 67°, Carstanjen [10] m. p. 69°.

2 : 6-*Dimethyl*-p-*benzoquinone.*—Recrystallisation from water–ethanol (8 : 1) gave bright yellow needles, m. p. 72° (sealed tube). Noelting and Baumann [11] give m. p. 72—73°.

*Bromanil.* Prepared as described by Graebe and Weltner [12] and recrystallised twice from benzene, this was obtained as lustrous deep yellow plates, m. p. (sealed tube) 300° (decomp.). Graebe and Weltner [12] give m. p. 300°.

*Iodanil.* Prepared as described by Torrey and Hunter [13] and repeatedly recrystallised from ethyl acetate to constant m. p., this quinone had m. p. (sealed tube) 290° (decomp.). Torrey and Hunter give m. p. 282—284°.

2 : 6-*Dichloro*-p-*benzoquinone.* Prepared as described by Faust [14] and crystallised twice from ethanol, this had m. p. 120°. Faust gives m. p. 120°.

*Chloro*-p-*benzoquinone.*—Prepared as described by Conant and Fieser [15] and recrystallised three times from ethanol, this formed orange prisms and a yellow amorphous powder, m. p. (both forms) 56·5°. Conant and Fieser give m. p. 57°.

*Duroquinone.*—Prepared as described by Smith [16] and recrystallised three times from aqueous ethanol, this formed yellow needles, m. p. 111°. Smith gives m. p. 109—110°, Nef [17] m. p. 111°.

*Method of Evaluating the Association Constants of the Interactions.*—The method described by McConnell and his co-workers,[4] which has been used to determine the association constants. It is fundamentally the same as those described by Benesi and Hildebrand [18] and Foster, Hammick, and Wardley,[19] except that allowance can be made in the first method for systems in which the absorption of the acceptor is measurable at the wavelength at which the determinations are made. In the system chloranil–hexamethylbenzene in carbon tetrachloride solution, the absorption of both components is zero at the wavelength of maximum absorption of the complex. This example thus permits a comparison to be made between the three methods when the determination is made at this wavelength. Some results are given in Table 1.

TABLE 1. *Extinction coefficient* ($\varepsilon_1$), *association constant* ($K$), *and free energy of formation* ($\Delta G$) *of the complex hexamethylbenzene–chloranil in carbon tetrachloride solution, determined by three methods from the same data.*

| | $\varepsilon_1$ (l. mole$^{-1}$ cm.$^{-1}$) | $K$ (l. mole$^{-1}$) | $\Delta G$ (kcal. mole$^{-1}$) |
|---|---|---|---|
| Benesi and Hildebrand | 2470 | 11·0 | −1·39 |
| Foster, Hammick, and Wardley | 2490 | 10·6 | −1·38 |
| McConnell and co-workers | 2510 | 10·7 | −1·37 |

The derivation of the function used to evaluate the association constant and the extinction coefficient of the complex given by McConnell and his co-workers [4] is not easy to follow. We give the following clarification.

The method can be applied only to systems in which the donor (*b*) does not absorb at the

[6] Graebe, *Annalen*, 1891, **263**, 19.
[7] Hassel and Naeshagen, *Z. phys. Chem.*, 1929, **6**, *B*, 445.
[8] Hammick, Hampson, and Jenkins, *J.*, 1938, 1263.
[9] Nietzki, *Ber.*, 1877, **10**, 834.
[10] Carstanjen, *J. pract. Chem.*, 1881, **23**, 423.
[11] Noelting and Baumann, *Ber.*, 1885, **18**, 1151.
[12] Graebe and Weltner, *Annalen*, 1891, **263**, 31.
[13] Torrey and Hunter, *J. Amer. Chem. Soc.*, 1912, **34**, 708.
[14] Faust, *Annalen*, 1869, **149**, 153.
[15] Conant and Fieser, *J. Amer. Chem. Soc.*, 1923, **45**, 2204.
[16] Smith, *Org. Synth.*, Coll. Vol. II, p. 254.
[17] Nef, *Ber.*, 1885, **18**, 2807.
[18] Benesi and Hildebrand, *J. Amer. Chem. Soc.*, 1949, **71**, 2703.
[19] Foster, Hammick, and Wardley, *J.*, 1953, 3817.

wavelength at which the measurements are made, though the acceptor ($a$) may absorb at this wavelength. If the optical density of a solution of the complex containing a total concentration of acceptor (*i.e.*, free and complexed) $= \alpha$ is $D$ cm.$^{-1}$, then $\bar{\varepsilon}$, the " formal extinction coefficient " of the solution, is defined by :

$$\bar{\varepsilon} = D/\alpha \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$\bar{\varepsilon}$ will become greater as $b$ is increased in accordance with the complexing equilibrium $a + b \rightleftharpoons c$.

The equilibrium constant for this interaction is given by

$$K = [c]/[a][b] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$[c]$, $[a]$, and $[b]$ represent the concentrations at equilibrium Now if $\varepsilon_0$ is the extinction coefficient of the acceptor, and $\varepsilon_1$ is the extinction coefficient of the complex, equation (1) gives :

$$D = \bar{\varepsilon}\alpha = \varepsilon_0[a] + \varepsilon_1[c] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

also

$$\alpha = [a] + [a][b]K = [a](1 + K[b]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

A function $Q$ may be defined such that :

$$Q = \frac{[b]}{(\bar{\varepsilon} - \varepsilon_0)} = \frac{1 + K[b]}{(\varepsilon_1 - \varepsilon_0)K}$$

from equations 2, 3, and 4. If $[b] \gg [a]$, then $[b]$ may be assumed to have the same value as the concentration of $b$ originally added.

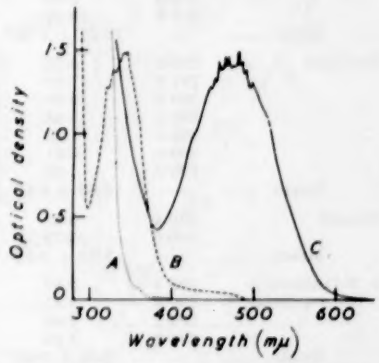



FIG. 1. *Absorption spectra in carbon tetrachloride of : A, hexamethylbenzene* (0·428M) ; *B,* 2 : 6-*dichloro-*p-*benzoquinone* (0·00335M) ; *C, a mixture of hexamethylbenzene* (0·428M) *and* 2 : 6-*dichloro-*p-*benzoquinone* (0·00335M).

Thus a plot of $Q$ against $[b]$ as abscissa should be linear, the gradient of the line being equal to $1/(\varepsilon_1 - \varepsilon_0)$ and the intercept with the $Q$ axis $1/(\varepsilon_1 - \varepsilon_0)K$, whence $K$ and $\varepsilon_1$ may be found.

Similarly if there is complexing of the type $ab_2$ present as well as of the type $ab$, then it may be shown that :

$$Q = \frac{1 + K_1[b] + K_2[b]^2}{(\varepsilon_1 - \varepsilon_0)K_1 + (\varepsilon_2 - \varepsilon_0)K_2[b]}$$

where $K_1$ is the equilibrium constant of the 1 : 1 complex, and $K_2$ that of the 1 : 2 complex, and $\varepsilon_1$ and $\varepsilon_2$ the extinction coefficients of the two complexes.

In none of the systems examined do the data yield significant values for $K_2[b]^2$ and it is therefore to be concluded that interactions other than 1 : 1 are negligible.

*Details of the Determination of the Association Constant and Extinction Coefficient of the Complex* 2 : 6-*Dichloro-*p-*benzoquinone–Hexamethylbenzene in Carbon Tetrachloride Solution.*—The McConnell method does not require that the measurements of optical density be made at the wavelength of maximum absorption of the complex. Nevertheless it is preferable to work at this wavelength, since there $D$ is usually a maximum for given concentrations of the two components. Also the value of the extinction coefficient of the complex is immediately obtainable, though in fact the charge-transfer bands do show some fine structure so that the wavelength of maximum absorption may not coincide with the centre of the band.

TABLE 2. *Data for the determination of the constants of the complex hexamethylbenzene–2 : 6-dichloro-p-benzoquinone in carbon tetrachloride solution.*

Master solutions: hexamethylbenzene 0·4919M; 2 : 6-dichloro-*p*-benzoquinone 0·00245M.
Temperature: 290·4° K. Wavelength: 480 mμ. $[a] = a = 0·00070$M.
Optical density of acceptor solution (0·00245M) was 0·016 cm.$^{-1}$, whence $\varepsilon_0 = 6·6$.

| $[b]$ (M) | $D$ (cm.$^{-1}$) | $D/a = \bar{\varepsilon}$ | $\bar{\varepsilon} - \varepsilon_0$ | $10^3\,[b]/(\bar{\varepsilon} - \varepsilon_0)$ | $[b]$ (M) | $D$ (cm.$^{-1}$) | $D/a = \bar{\varepsilon}$ | $\bar{\varepsilon} - \varepsilon_0$ | $10^3\,[b]/(\bar{\varepsilon} - \varepsilon_0)$ |
|---|---|---|---|---|---|---|---|---|---|
| 0·0703 | 0·274 | 391·6 | 385·0 | 0·1826 | 0·2109 | 0·607 | 867·6 | 861·0 | 0·2452 |
| 0·1054 | 0·371 | 530·3 | 523·7 | 0·2013 | 0·2460 | 0·659 | 941·7 | 935·1 | 0·2632 |
| 0·1406 | 0·457 | 652·7 | 646·1 | 0·2178 | 0·2812 | 0·708 | 1012·0 | 1005·4 | 0·2799 |
| 0·1757 | 0·531 | 579·1 | 752·5 | 0·2334 | 0·3515 | 0·807 | 1153·0 | 1146·4 | 0·3069 |

TABLE 3. *Summarised results for association constants (K), free energies of formation (ΔG), molar extinction coefficients ($\varepsilon_1$), and wave-numbers (ν) of the maxima of the charge-transfer band-envelopes of hexamethylbenzene–substituted* p*-benzoquinone complexes in carbon tetrachloride solution.*

| Acceptor | Temp. (°K) | $K$ (l./mole) | $\Delta G$ (kcal./mole) | $\varepsilon_1$ | $\nu$ (cm.$^{-1}$) | Reduction potential [a] (v) |
|---|---|---|---|---|---|---|
| Chloranil | 291·0° | 10·79 | −1·375 | 2502 | | |
| | 291·5 | 10·91 | −1·333 | 2540 | | |
| | 291·0 | 10·33 | −1·350 | 2528 | | |
| | 291·5 | 10·50 | −1·361 | 2517 | | |
| | 291·5 | 10·81 | −1·377 | 2487 | | |
| | 289·0 | 9·83 | −1·252 | 2732 | | |
| | 291·0 | 10·64 | −1·366 | 2522 | 19,300 [b] | 0·742 |
| Means ..... | — | 10·27 ± 0·38 [b] | −1·345 ± 0·040 [b] | 2548 ± 77 [b] | | |
| Bromanil | 289·0 | 5·84 | −1·013 | 2325 | | |
| | 291·9 | 7·02 | −1·129 | 1822 | | |
| | 290·8 | 6·09 | −1·044 | 2070 | | |
| | 292·2 | 5·88 | −1·016 | 2627 | | |
| | 290·0 | 7·33 | −1·147 | 1666 | | |
| | 290·0 | 6·81 | −1·105 | 1725 | | |
| | 290·0 | 7·63 | −1·170 | 1620 | 18,980 | 0·746 |
| Means ..... | — | 6·66 ± 0·69 | −1·091 ± 0·059 | 1979 ± 351 | | |
| Iodanil | 289·4 | 3·51 | −0·728 | 1541 | | |
| | 290·0 | 3·72 | −0·757 | 1366 | 19,570 | — |
| Means ..... | — | 3·62 ± 0·10 | −0·742 ± 0·015 | 1454 ± 88 | | |
| 2 : 6-Dichloro-*p*-benzoquinone | 290·4 | 2·87 | −0·606 | 2273 | | |
| | 290·4 | 2·81 | −0·597 | 2276 | | |
| | 292·2 | 2·42 | −0·513 | 2408 | | |
| | 292·2 | 2·28 | −0·480 | 2516 | 20,830 | 0·740 |
| Means ..... | — | 2·60 ± 0·25 | −0·549 ± 0·054 | 2370 ± 101 | | |
| Chloro-*p*-benzoquinone | 292·0 | 1·45 | −0·218 | 1838 | | |
| | 291·0 | 1·27 | −0·137 | 2087 | | |
| | 291·0 | 1·38 | −0·184 | 1978 | 22,620 | 0·734 |
| Means ..... | — | 1·37 ± 0·08 | +0·180 ± 0·033 | 1968 ± 102 | | |
| *p*-Benzoquinone | 290·8 | 0·61 | +0·286 | 1944 | | |
| | 291·6 | 0·56 | +0·336 | 2089 | 23,920 | 0·711 |
| Means ..... | — | 0·58 ± 0·02 | +0·311 ± 0·025 | 2016 ± 73 | | |
| Methyl-*p*-benzoquinone | 291·2 | 0·49 | +0·440 | 1820 | 24,450 | 0·653 |
| | 291·0 | 0·51 | +0·395 | 1732 | | |
| Means ..... | — | 0·50 ± 0·01 | +0·418 ± 0·022 | 1776 ± 44 | | |
| 2 : 6-Dimethyl-*p*-benzoquinone | 288·8 | 0·35 | +0·599 | 2117 | | |
| | 289·0 | 0·34 | +0·622 | 2141 | 25,640 | 0·607 |
| Means ..... | — | 0·34 ± 0·01 | +0·610 ± 0·012 | 2129 ± 12 | | |
| Duroquinone | 289·0 | 0·32 | +0·665 | 1414 | | |
| | 288·0 | 0·50 | +0·405 | 969 | | |
| | 290·0 | 0·42 | +0·522 | 1145 | 25,440 | — |
| Means ..... | — | 0·41 ± 0·07 | +0·531 ± 0·106 | 1176 ± 183 | | |

[a] Relative potentials in benzene solution determined by Hunter and Kvalnes (*J. Amer. Chem. Soc.*, 1932, **54**, 2878) and Kvalnes (*ibid.*, 1934, **56**, 668, 671). [b] Briegleb and Czekalla [3] give $K = 9·25$ l. mole$^{-1}$, $\Delta G = -1·36$ kcal. mole$^{-1}$, $\nu = 19{,}350$ cm.$^{-1}$, and $\varepsilon_1 = 2750$.

Three separate spectra are measured (cf. Fig. 1) : (1) the spectrum of the donor, hexamethylbenzene, in carbon tetrachloride (this shows that the absorption is negligible above 360 mμ); (2) the spectrum of the acceptor, 2 : 6-dichloro-*p*-benzoquinone in carbon tetrachloride, from which $\varepsilon_0$ may be calculated; and (3) the spectrum of a mixture of donor and acceptor in carbon tetrachloride in which $[a] \ll [b]$ (this shows a new band with a maximum at about 480 mμ).

Two master solutions were prepared, one of pure acceptor, the other of pure donor, and from them eight solutions, containing a fixed concentration of acceptor and varying amounts of donor were made up volumetrically into calibrated flasks. Each solution had a large donor concentration relative to that of acceptor. The optical densities ($D$) of this set of solutions were then measured at 480 mμ, by means of a Unicam S.P. 600 Spectrophotometer. The results of a typical determination are given in Table 2. The linear relation between $Q$ and $b$ was determined statistically by the method of least squares, whence the gradient $= 4{\cdot}41 \times 10^{-4}$ cm. mole l.$^{-1}$, and the intercept with the $Q$ axis $= 1{\cdot}56 \times 10^{-4}$ cm. mole$^2$ l.$^{-2}$.

As $\varepsilon_0 = 6{\cdot}6$ l. mole$^{-1}$ cm.$^{-1}$, $\varepsilon_1 = 2276$ l. mole$^{-1}$ cm.$^{-1}$, and $K = 2{\cdot}82$ l. mole$^{-1}$.

The results of all the determinations are summarised in Table 3.

## Discussion

The free energies of formation of the hexamethylbenzene–substituted *p*-benzoquinone complexes are not linearly related to the reduction potentials of the quinones themselves

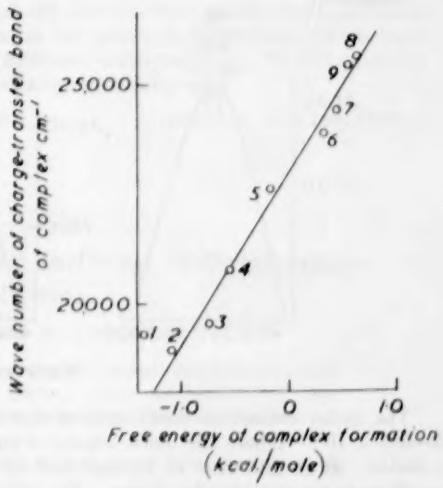



Fig. 2. *Relation between the free energy of complex formation* ($\Delta G$) *and the wave-number of the charge-transfer band* ($\nu$) *for the series of hexamethylbenzene–substituted* p*-benzoquinone complexes in carbon tetrachloride.* **1**, *Chloranil*; **2**, *bromanil*; **3**, *iodanil*; **4**, 2 : 6-*dichloro*-p-*benzoquinone*; **5**, *chloro*-p-*benzoquinone*; **6**, p-*benzoquinone*; **7**, *methyl*-p-*benzoquinone*; **8**, 2 : 6-*dimethyl*-p-*benzoquinone*; **9**, *duroquinone*.

(cols. 4 and 7 of Table 3). This is to be expected since the free energies of formation of the complexes are the sum of the contributions due to polarisation, London, van der Waals, and other such forces, further stabilised by resonance with a structure in which one, or perhaps two, electrons have been donated from the donor to the acceptor molecule. The reduction potentials of the quinones on the other hand are a measure of the free energies involved in the acceptance of a pair of hydrogen atoms. Nevertheless the free energies of formation of the quinone complexes derived from our determinations of equilibrium constants are in approximately the same order as the reduction potentials of the corresponding *p*-benzoquinones.

It is seen that the energy of excitation of each complex as measured by the wave-number of the central peak of the charge-transfer band is proportional to the free energy of formation of the complex (Fig. 2). This may be explained in terms of Mulliken's [1] description of this class of complex. The ground state of the complex is $\psi_N$ where :

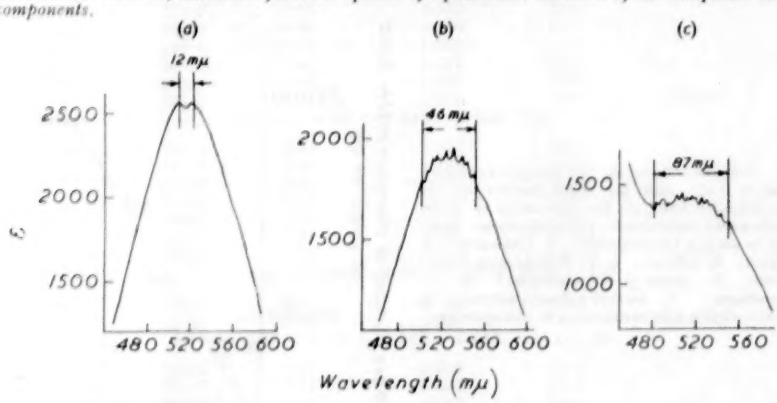
$$\psi_N = x\psi(a, b) + y\psi(a^-b^+)$$

$a$ and $b$ represent the electron donor and the electron acceptor respectively. $\psi(a, b)$ is a no-bond function, and $\psi(a^-b^+)$ is the dative function in which an electron has been donated from $b$ to $a$. An excited state $\psi_E$ exists where :

$$\psi_E = x^*\psi(a^-b^+) - y^*\psi(a, b)$$

Excitation corresponds to the transition $\psi_N \longrightarrow \psi_E$. As the energy of excitation (measured by the wave-number of the maximum of the charge-transfer band) is large compared with the energy of the ground state, and as $x^* \gg y^*$ normally, the excitation energy within this series of complexes may be said, to a first approximation, to be proportional to the energy of the excited state, which is mainly the structure $\psi(a^-b^+)$. If in the ground state, either $x \ll y$, indicating that the ground state is essentially ionic, which is unlikely in the complexes being studied here, or, alternatively, the contribution of the no-bond function is present as a more or less constant fraction in the series of complexes, then the differences in the energy of the ground state (measured by the free energy of complex formation) may be attributed to the relative contribution of the dative structure $\psi(a^-b^+)$. This would account for the proportionality between the free energies of formation of the complexes and their excitation energies.

FIG. 3. *Absorption spectra of hexamethylbenene with (a) chloranil, (b) bromanil, and (c) iodanil in carbon tetrachloride solution, calculated from the spectra of equilibrium mixtures of the complexes with their components.*




The molar extinction coefficients of the complexes appear to be mainly of the order $2—2{\cdot}5 \times 10^3$. Where the steric effects of the complexes might be expected to be large, however, as in the case of iodanil and of duroquinone, the values of the extinction coefficients are considerably lower. The molar extinction coefficients for the hexamethylbenzene complexes of 2 : 6-dichloro- and 2 : 6-dimethyl-*p*-benzoquinone are higher than for the corresponding monosubstituted quinones, in which the steric effects would be expected to be less. It is interesting to note that both chloro-*p*-benzoquinone and toluquinone have low melting points. This suggests that these monosubstituted *p*-benzoquinones do not form very stable crystal lattices, which again may be due to the steric effects of their unsymmetrical molecules.

The charge-transfer spectra of most of the complexes measured show some fine structure similar to that of the hexamethylbenzene–2 : 6-dichloro-*p*-benzoquinone complex shown in Fig. 1. This has been found to be reproducible on different intruments and persists at low optical densities, which suggests that it is not an instrumental effect. In the case of the hexamethylbenzene–chloranil complex this observation of fine structure is in disagreement with the description given by Briegleb and Czekalla [3] of the same complex (also in carbon tetrachloride solution). They find only one maximum in the charge-transfer band, at 19,350 cm.$^{-1}$ which agrees well with the centre of the band-envelope obtained in our determination, namely, 19,300 cm.$^{-1}$. In the series of complexes of hexamethylbenzene

with chloranil, bromanil, and iodanil, the band-width of the fine structure increases progressively (Fig. 3). The energies corresponding to these band-widths are proportional to the atomic excitation $^2P_{3/2} - {}^2P_{1/2}$ of the corresponding halogen atoms [20] (Table 4). However it seems unlikely that this correspondence could be given the same explanation as in

TABLE 4. *Energies corresponding to the band-width of the fine structure in the charge-transfer bands of certain complexes.*

| | Atomic excitation [20] $^2P_{3/2} - {}^2P_{1/2}$ (ev) | Band-width of fine structure in tetrahalogeno-*p*-benzoquinone–hexamethylbenzene complexes (mμ) | Energy corresponding to band-widths in col. 3 (ev) |
|---|---|---|---|
| Chlorine ..... | 0·109 | 12 | 0·056 |
| Bromine ..... | 0·454 | 46 | 0·21 |
| Iodine ..... | 0·937 | 87 | 0·42 |

the spectra of the alkali halides, for the separation of the peaks in the halide spectra is thought to be due to the formation of free halogen atoms during absorption, the two peaks corresponding to the production of halogen atoms in either the $^2P_{3/2}$ or the $^2P_{1/2}$ state.[20,21] The facts that the quinone complexes have spectra which show more than two peaks in the charge-transfer band and that hexamethylbenzene–2 : 6-dichloro-*p*-benzoquinone shows a band-width of fine structure of 28 mμ are difficult to interpret. Also the presence of fine structure in the charge-transfer band of the *p*-benzoquinone complex would require another explanation. It seems more likely that the fine structure results from electronic transitions corresponding to energy transitions in the quinones themselves, which have become modified by the proximity of the donor molecule in the complex. No fine structure has been observed in the case of the methyl-*p*-benzoquinone complexes.

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[20] Turner, *Phys. Rev.*, 1926, **27**, 397.
[21] Orgel, *Quart. Rev.*, 1954, **8**, 423.

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## 756. *The Reaction of Oximes with* iso*Propyl Methylphosphonofluoridate* (*Sarin*).

By A. L. GREEN and B. SAVILLE.

In neutral or slightly alkaline aqueous solution, oximes react rapidly with *iso*propyl methylphosphonofluoridate (Sarin). The mechanism of the reaction and the effect of structure on the reactivity of different oximes are discussed.

The dissociation constants of thirteen oximes have been measured at 25° in 0·1M-aqueous potassium chloride.

MANY organophosphorus compounds such as phosphorofluoridates, pyrophosphates, and *p*-nitrophenyl phosphates are potent inhibitors of the enzyme cholinesterase.[1] Inhibition by these compounds cannot be reversed by dilution or dialysis,[1] but hydroxylamine [2] and some of its derivatives, in particular hydroxamic acids [3] and oximes,[4] will restore the activity of the inhibited enzyme. Lately it has been shown [5] that hydroxamic acids react rapidly in neutral aqueous solution with di*iso*propyl phosphorofluoridate (DFP) and with *iso*propyl methylphosphonofluoridate (Sarin), two of the more powerful organophosphorus anticholinesterases.[6] The present paper describes the analogous reaction between oximes and Sarin.

[1] Evidence reviewed by Nachmansohn and Wilson, *Adv. Enzymology*, 1951, **12**, 259.
[2] Wilson, *J. Biol. Chem.*, 1951, **190**, 111.
[3] Wilson and Meislich, *J. Amer. Chem. Soc.*, 1953, **75**, 4628.
[4] Childs, Davies, Green, and Rutland, *Brit. J. Pharmacol.*, 1955, **10**, 462.
[5] Hackley, Plapinger, Stolberg, and Wagner-Jauregg, *J. Amer. Chem. Soc.*, 1955, **77**, 3651.
[6] Michel, *Fed. Proc.*, 1955, **14**, 255.

The compounds studied most extensively were 1 : 2-dione monoximes (I) since these were among the more active members of the group in nearly neutral solution. Evidence for the nature of the reaction between these oximes and Sarin was obtained in several ways.

(I) R·CO·CR′:N·OH (R = alkyl or aryl, R′ = H or alkyl)

For each mole of Sarin decomposed (as verified by Marsh and Neale's colorimetric method [7]) it was found that one mole of oxime (determined by its yellow colour in alkaline solution) was consumed. For each mole of oxime (I) consumed, one mole of the carboxylic acid $R{\cdot}CO_2H$ was formed (see Experimental for R = Ph, R′ = H). Hydrogen cyanide was also formed from 2-oxo-aldoximes (I; R′ = H) but not from the corresponding ketoximes (I; R′ = alkyl). The reactions were accompanied by the liberation of 3 mols. of acid titratable to pH 6—8: one of these three is the carboxylic acid $R{\cdot}CO_2H$, and the other two must result from the splitting of the phosphonofluoridate.

The overall reaction may be expressed by the equation:

$$R{\cdot}CO{\cdot}CR'{:}N{\cdot}OH + Me{\cdot}PFO{\cdot}OPr^i + H_2O \longrightarrow R{\cdot}CO_2H + R'CN + HF + Me{\cdot}PO(OH){\cdot}OPr$$

In the presence of a large excess of oxime the rate of total acid production was found to obey a first-order law, the rate being proportional to the concentration of the oxime anion. It is therefore probable that the reaction involves a rate-determining *O*-phosphorylation of the oxime anion (step 1), followed by rapid decomposition of the oxime phosphonate to the observed products, by a step such as (2):

(1) $R{\cdot}CO{\cdot}CR'{:}N{\cdot}O^- + Me{\cdot}PFO{\cdot}OPr^i \longrightarrow R{\cdot}CO{\cdot}CR'{:}N{\cdot}O{\cdot}PMeO{\cdot}OPr^i + F^-$ (slow)
(II)

(2) $HO^- + R{\cdot}CO{-}CR'{=}N{-}O{\cdot}PMeO{\cdot}OPr^i \longrightarrow R{\cdot}CO_2H + R'{\cdot}CN + Me{\cdot}PO(OPr^i){\cdot}O^-$ (fast)

The equally rapid formation of 3 mols. of acid from Sarin with either 2-oxo-aldoximes (I; R′ = H) or ketoximes (I; R′ = alkyl) makes it unlikely that 2-oxo-aldoxime phosphonates (II; R′ = H) decompose by initial elimination of *iso*propyl methylphosphonic acid to give an acyl cyanide.

The acylating properties of the postulated oxime phosphonate (II) have been shown by performing the reaction between Sarin and hydroxyiminoacetone (I; R = Me, R′ = H) in the presence of aniline, acetanilide being formed, presumably as follows:

$$Ph{\cdot}NH_2 + Ac{\cdot}CH{:}N{\cdot}O{\cdot}PMeO{\cdot}OPr^i \longrightarrow Ph{\cdot}NHAc + HCN + Me{\cdot}PO(OH){\cdot}OPr^i$$

The reaction of Sarin with hydroxyiminoacetylacetone (I; R = Me, R′ = Ac), in which the oxime group is flanked by two acyl groups instead of one, was more complicated. Although at moderately high pH (8·5) the expected 3 mols. of acid were formed, in neutral and more acid solutions (pH 6·5) over 6 mols. of acid were formed and about 3 mols. of oxime were consumed. Hydroxyiminoacetylacetone itself is slowly decomposed in neutral aqueous solution (see Figure). Pyruvic acid was found among the products of both the spontaneous and the Sarin-accelerated decomposition but the mechanism is obscure and was not further investigated.

*Rates of Reaction between Oximes and Sarin.*—A preliminary study has been made of the reactivity of Sarin with a number of oximes by measurement of the rate of acid production by continuous titration to constant pH with sodium hydroxide.*

In the presence of a large excess of oxime, the observed rate of total-acid production was of the first order and proportional to the oxime concentration and to the degree of ionisation, *i*, of the oxime calculated from the Henderson–Hasselbalch equation (see Table

* A more detailed kinetic study of the reaction between oximes and organophosphorus anticholinesterases generally, in which the rate of disappearance of the anticholinesterase was measured directly, will be published later. The rates obtained by this method for the reaction of oximes with Sarin agree quite well with those obtained here by means of the acid production.

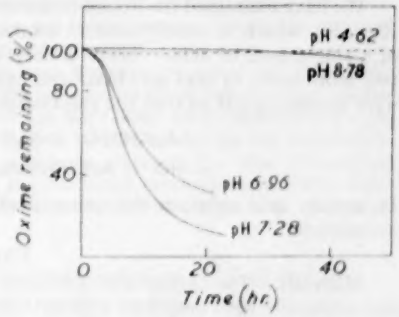
[7] Marsh and Neale, *Chem. and Ind.*, 1956, 494.

1), *i.e.*, $-d[Sarin]/dt = d[nH^+]/dt = k_2 i[A][Sarin]$, where $n$ is the number of moles of acid obtained per mole of Sarin decomposed and [A] is the oxime concentration.

TABLE 1. *Second-order rate constants* (*l. mole*$^{-1}$ *min.*$^{-1}$) *for the reaction of hydroxyiminoacetone* ($pK_a$ 8·30) *with Sarin at* 25°.

| | | | |
|---|---|---|---|
| pH | 7·4 | 7·6 | 7·8 |
| Apparent rate constant ($= ik_2$) | 27·8 | 45 | 57·9 |
| Anion (%) ($= 100i$) | 11·2 | 16·6 | 24 |
| $k_2$ | 248 | 271 | 242 |

Table 2 shows the anion rate constants ($k_2$) for a number of 1 : 2-dione monoximes, salicylhydroxamic acid, and some substituted benzaldoximes. With simple aldoximes 1—2 mols. of acid are produced, again at a first-order rate, but the nature of the products was not investigated. The main general tendency, for all the compounds, is an increase of reactivity with increasing $pK_a$, *i.e.*, the greater the affinity of the anion for a proton, the




*Stability of hydroxyiminoacetylacetone in buffer solutions at various* pH's.

greater its reactivity with a phosphoryl centre. For compounds with about the same $pK_a$, *e.g.*, hydroxyiminoacetylacetone, salicylhydroxamic acid, and 2-hydroxyiminomethylpyridine methiodide, even a large variation in structure of the substituent on the N·O$^-$ ion has surprisingly little effect on the reactivity. For the 2-oxo-ketoximes (I; R = Me, R′ = Me—Pr$^i$) the $pK_a$ effect is modified by increase in the size of the alkyl radical which

TABLE 2. *Second-order rate constants* (*l. mole*$^{-1}$ *min.*$^{-1}$) *for the reaction of oxime anions with Sarin at* 25°.

| Compound | $pK_a$ | $k_2$ |
|---|---|---|
| Hydroxyiminoacetone (I; R = Me, R′ = H) | 8·30 | 250 |
| 2-Oxo-*n*-butyraldoxime (I; R = Et, R′ = H) | 8·37 | 240 |
| Hydroxyiminoacetophenone (I; R = Ph, R′ = H) | 8·25 | 140 |
| Diacetyl monoxime (I; R = Me, R′ = Me) | 9·30 | 410 |
| 3-Hydroxyiminopentan-2-one (I; R = Me, R′ = Et) | 9·38 | 340 |
| 3-Hydroxyimino-4-methylpentan-2-one (I; R = Me, R′ = Pr$^i$) | 9·50 | 310 |
| Hydroxyiminoacetylacetone (I; R = Me, R′ = Ac) | 7·38 | 80 |
| Salicylhydroxamic acid | 7·43 | 130 |
| Salicylaldoxime | 9·17 | 1490 |
| *p*-Hydroxybenzaldoxime | 8·93 | 30 |
| 2-Hydroxyiminomethylpyridine | 10·10 | 1690 |
| 2-Hydroxyiminomethylpyridine methiodide | 7·82 | 120 |
| 3-Hydroxyiminomethylpyridine methiodide | 9·10 | 990 |
| 4-Hydroxyiminomethylpyridine methiodide | 8·23 | 380 |

causes a drop in the reactivity despite a slight increase in $pK_a$. The very low reactivity of *p*-hydroxybenzaldoxime is almost certainly due to ionisation of the phenolic hydroxyl group rather than of the hydroxyimino-group. Acetylation of *p*-hydroxybenzaldoxime gives an aryl acetate whereas that of salicylaldoxime gives an oxime acetate owing to protection of the phenolic hydroxyl group by chelation with the nitrogen atom in the oxime.[8] Monophenolic compounds are known to react slowly with phosphonofluoridates.[9]

[8] Brady, *J.*, 1931, 105.
[9] Jandorf, Wagner-Jauregg, O'Neill, and Stolberg, *J. Amer. Chem. Soc.*, 1952, **74**, 1521.

*Reaction of Oximes with Other Acid Anhydrides.*—The organophosphorus anticholinesterases may be regarded as acid anhydrides, either simple, such as tetraethyl pyrophosphate which is the anhydride of *OO*-diethylphosphoric acid, or mixed, such as Sarin which may be looked upon as a mixed anhydride of *P*-methyl-*O*-*iso*propylphosphonic acid and hydrofluoric acid. The oximes are not specific nucleophilic reagents for phosphoric anhydrides but will also react rapidly with related compounds such as sulphonyl halides and acetic anhydride. Thus Darzens and Mentzer [10] have used the action of thionyl chloride on 2-oxo-alkyl phenyl ketoximes (I; R = Ph, R′ = alkyl) as a preparative method for alkyl cyanides (R′·CN), and Werner and Piguet [11] found that an alkaline aqueous solution of benzil α-monoxime (I; R = R′ = Ph) with benzenesulphonyl chloride gave benzoic acid and benzonitrile:

$$Ph\cdot CO\cdot CR'{:}N\cdot OH + SOCl_2 + H_2O \longrightarrow Ph\cdot CO_2H + R'\cdot CN + SO_2 + 2HCl$$

$$Ph\cdot CO\cdot CPh{:}N\cdot OH + Ph\cdot SO_2Cl + H_2O \longrightarrow Ph\cdot CO_2H + Ph\cdot CN + Ph\cdot SO_3H + HCl$$

We have examined the action of acetic anhydride on hydroxyiminoacetone (I; R = Me, R′ = H), which in nearly neutral solution occurs almost instantaneously with liberation of a single mol. of acid. There is then a slower breakdown of the oxime acetate to give two more mols. of acid and hydrogen cyanide. The latter step occurs much more rapidly with increasing pH so that the reaction sequence is presumably:

$$Ac\cdot CH{:}N\cdot O^- + Ac_2O \longrightarrow Ac\cdot CH{:}N\cdot OAc + AcO^-$$

$$HO^- + Ac\cdot CH{:}N\cdot OAc \longrightarrow 2AcO^- + HCN + H^+$$

In weakly acid solution the oxime acetate is relatively stable but with aniline it gives acetanilide.

## Experimental

*Materials.*—The oximes used are listed in Table 3. The aldoxime methiodides which have not previously been described were obtained by boiling the aldoximes in ethanol for 4 hr. with two mols. of methyl iodide.

Table 3.

| Compound and method | Solvent * | M. p. | M. p. (lit.) | Calc. (%) N | Found (%) N |
|---|---|---|---|---|---|
| Hydroxyiminoacetone [12] | V.s. | 65—66° | 68° [12] | 16·1 | 15·9 |
| 2-Oxo-*n*-butyraldoxime [13] | V.s. | 55 | 55 [13] | 13·9 | 14·5 |
| Hydroxyiminoacetophenone [14] | $CHCl_3$ | 124—126 | 126—128 [14] | — | — |
| Diacetyl monoxide [15] | $CHCl_3$–Pet | 73—75 | 75 [16] | — | — |
| 3-Hydroxyiminopentan-2-one [15] | V.s. | 52—54 | 53—55 [17] | 12·2 | 12·7 |
| 3-Hydroxyimino-4-methylpentan-2-one [15] | Pet | 78—80 | 75 [18] | 10·9 | 11·2 |
| Hydroxyiminoacetylacetone [19] | V.s. | 73—75 | 75 [19] | — | — |
| Salicylhydroxamic acid [20] | MeOH | 165 | 168—169 [21] | — | — |
| Salicylaldoxime [21] | $CHCl_3$–Pet | 57 | 57 [22] | — | — |
| *p*-Hydroxybenzaldoxime [21] | $C_6H_6$ | 114—115 | 112 [23] | 10·2 | 10·8 |
| 2-Hydroxyiminopyridine [21] | $H_2O$ | 111 | 113 [24] | 22·9 | 22·8 |
| | | | | I | I |
| *2-Hydroxyiminomethylpyridine methiodide* | Aq. EtOH | 218—220 | — | 48·0 | 47·7 |
| *3-Hydroxyiminomethylpyridine methiodide* | EtOH | 152—154 | — | 48·0 | 47·7 |
| *4-Hydroxyiminomethylpyridine methiodide* | EtOH | 171—173 | — | 48·0 | 47·7 |

* V.s. = purified by vacuum-sublimation; pet = light petroleum (b. p. 60—80°).

[10] Darzens and Mentzer, *Compt. rend.*, 1941, **213**, 268.
[11] Werner and Piguet, *Ber.*, 1904, **37**, 4295.
[12] Freon, *Ann. Chim.* (*France*), 1939, **11**, 460.
[13] Sharp and Spring, *J.*, 1948, 1862.
[14] Claisen and Manasse, *Ber.*, 1887, **20**, 2194.
[15] Diels and Jost, *Ber.*, 1902, **35**, 3292.
[16] Kalischer, *Ber.*, 1895, **28**, 1518.
[17] Meyer and Zublin, *Ber.*, 1878, **11**, 323.
[18] Westenberger, *Ber.*, 1883, **16**, 2991.
[19] Wolff, *Annalen*, 1902, **325**, 139.
[20] Jeanrenaud, *Ber.*, 1889, **22**, 1273.
[21] Hickinbottom, "Reactions of Organic Compounds," Longmans Green, London, 1945, p. 137.
[22] Lach, *Ber.*, 1883, **16**, 1782.
[23] Dollfus, *Ber.*, 1892, **25**, 1925.
[24] Lenart, *Ber.*, 1914, **47**, 809.

*Dissociation Constants.*—These were determined by potentiometric titration with 0·1N-sodium hydroxide of the oxime (about 0·01M) in aqueous potassium chloride (0·1M) at 25°. The potassium chloride was used to maintain an approximately constant ionic strength. The $pK_a$ values were calculated by the Henderson–Hasselbalch equation from pH's around the half-neutralisation points.

*Kinetic Measurements.*—The reactions were carried out at 25° in a small jacketed beaker fitted with a magnetic stirrer and containing a glass electrode. A calomel electrode immersed in saturated aqueous potassium chloride at 25° was connected to the reaction vessel by a glass salt bridge fitted with a Polythene capillary tube dipping into the reaction solution. A slow syphoning of liquid through the salt bridge was controlled by an ungreased glass tap. The two electrodes were connected to an E.E.L. Model 23 pH meter. A solution of Sarin (0·05M) in "AnalaR" propan-2-ol (0·1 ml.) was added to the oxime (0·01—0·1M) in aqueous potassium chloride (5 ml.; 0·1M), neutralised to the required pH with sodium hydroxide. The pH was maintained constant during the reaction by frequent addition of sodium hydroxide (0·1N) from an "Agla" micro-syringe fitted with a Polythene outlet tube dipping into the reaction mixture. Sufficient alkali was introduced at each addition to raise the pH slightly above the value required. The time was then recorded at which the pH-meter needle passed the required value. Generally the pH during the reaction was maintained within ±0·05 unit.

The first-order rate constants (the oxime being in large excess) were calculated graphically from the relation $k_{obs.} = k_2 i[A] - k_{solv.} = (1/2{\cdot}303t) \log [a/(a - x)]$ where $a$ is the total volume of alkali required to neutralise all the acid formed and $x$ is the volume added after time $t$. [A] is the concentration of the oxime, and $i$ the fraction ionised as calculated from the Henderson–Hasselbalch equation. The small spontaneous solvolysis rate, $k_{solv.}$, was determined independently over the pH range (6·5—9) used for the reactivity measurements. The slight dilution during the reaction due to the volume of the added alkali was neglected. A sample experiment is shown in Table 4.

TABLE 4. *Reaction of Sarin with hydroxyiminoacetone* (0·01M) *at* pH 7·80 *and* 25°.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $t$ (sec.) | 0 | 38 | 72 | 100 | 149 | 190 | ∞ |
| $x$ (μl.) | 0 | 40 | 70 | 90 | 110 | 120 | 144 |
| $a - x$ | 144 | 104 | 74 | 54 | 34 | 24 | |
| log $(a - x)$ | 2·158 | 2·017 | 1·869 | 1·732 | 1·532 | 1·380 | |

Total volume of sodium hydroxide (0·1N) = 0·144 ml. Since this exactly neutralises the acid from 0·1 ml. of Sarin (0·05M), approx. 3 moles of acid are produced per mole of Sarin decomposed. From a graph of log $(a - x)$ against $t$, $k_{obs.} = 0{\cdot}582$ min.$^{-1}$. At pH 7·8, $k_{solv.} = 0{\cdot}003$ min.$^{-1}$, hence $k_2 i[A] = 0{\cdot}579$, and $k_2 i = 57{\cdot}9$ l. mole$^{-1}$ min.$^{-1}$. Since $i = 1/\{1 + \text{antilog } (pK_a - pH)\} = 0{\cdot}24$, $k_2 = 242$ l. mole$^{-1}$ min.$^{-1}$.

The reaction between hydroxyiminoacetone and acetic anhydride (in acetone) was studied similarly, but the rate of acid formation was too rapid to enable a rate constant to be obtained.

On completion of the reaction between Sarin and several of the 2-oxo-aldoximes the presence of a molar equivalent of cyanide ion was shown by conversion with bromine water into cyanogen bromide which was estimated by the intense red colour given with benzidine in pyridine.[23] No free cyanide ion could be detected by this method among the products of the reaction between Sarin and 2-oxo-ketoximes.

*Disappearance of Oxime.*—Solutions of 2-oxo-oximes in aqueous sodium hydroxide (0·01M) show a linear relation between concentration (up to at least 0·001M) and absorption density measured on a Hilger "Spekker" absorptiometer (601 Spectrum Violet filter). Colorimetric estimation of the oxime in samples taken at the beginning and end of a reaction at pH 7·4 between Sarin (0·002M) and hydroxyiminoacetophenone (0·01M) showed that one mole of oxime was consumed per mole of Sarin. However, in a corresponding reaction between Sarin and hydroxyiminoacetylacetone approximately 3 moles of oxime decomposed per mole of Sarin.

*Decomposition of Hydroxyiminoacetylacetone.*—The rate of spontaneous decomposition of this oxime at different pH's (see Figure) was determined colorimetrically as described above. For the more acidic buffer it was advantageous to separate the oxime from the buffer with ether and then to extract the oxime from the ether with 10% aqueous sodium carbonate. When the decomposition in the neutral buffers was complete, pyruvic acid (as its 2 : 4-dinitrophenylhydrazone) was isolated from the products in a way similar to that described below.

*Formation of Pyruvic Acid from Hydroxyiminoacetylacetone.*—A solution of the oxime (1·29 g., 0·01 mole) and Sarin (0·14 g., 0·001 mole) in aqueous disodium hydrogen phosphate (0·1M; 250 ml.) was set aside at 25° for 2 days. The mixture was made alkaline with 10%

aqueous sodium hydroxide and washed with chloroform to remove traces of non-acidic material. The aqueous solution was acidified (10% hydrochloric acid) to about pH 1 and washed with ether. Evaporation of the ether layer gave a residue containing no ketone but which smelt of acetic acid and gave an ester with ethanol and sulphuric acid. The residual acidic aqueous solution, after partial evaporation under reduced pressure to expel dissolved ether, was treated with 2 : 4-dinitrophenylhydrazine in hydrochloric acid (2N). A copious yellow precipitate was obtained, which after crystallisation from acetic acid melted at 214° alone or mixed with pyruvic acid 2 : 4-dinitrophenylhydrazone.

*Formation of Benzoic Acid from Hydroxyiminoacetophenone.*—A solution of Sarin (0·05M) in propan-2-ol (10 ml.) was added to the oxime (0·01M) in aqueous disodium hydrogen phosphate (0·1M; 50 ml.). After 18 hr. the solution was acidified with hydrochloric acid (1N; 10 ml.) and extracted with chloroform. The chloroform solution was washed with water, dried ($MgSO_4$), and evaporated. A slightly yellow crystalline solid (52 mg.; m .p. 100—104°) was obtained which crystallised from water to give benzoic acid in white needles, m. p. and mixed m. p. 119—121°.

*Formation of Acetanilide.*—(*a*) Acetic anhydride (2 ml.) was added to hydroxyiminoacetone (0·87 g.). The solid dissolved without generation of heat. After being warmed to 30—40° for 1 hr. the mixture was poured into water (100 ml.) and after a further hour aniline (3 ml.) was added to the solution. When shaken, the aniline dissolved, but the solution soon became cloudy with the formation of an oily emulsion. Hydrochloric acid was added, and the oil was extracted with ether. The ethereal solution was washed with aqueous sodium carbonate to remove residual oxime, dried ($MgSO_4$), and evaporated to pale brown crystals (0·55 g.), m. p. 100—104°. Recrystallisation from aqueous alcohol gave acetanilide as plates, m. p. and mixed m. p. 114°. Repetition of this experiment in the absence of the oxime gave no acetanilide, showing that this compound is not formed by reaction of aniline with incompletely hydrolysed acetic anhydride. Aniline does not react with this oxime alone. (*b*) Sarin (0·28 g.) was added to a solution of hydroxyiminoacetone (1·0 g.) and sodium hydroxide (0·4 g.) in water (100 ml.) previously saturated with aniline. After ½ hr. extraction with ether as described in (*a*) again gave a moderate yield of acetanilide.

CHEMICAL DEFENCE EXPERIMENT ESTABLISHMENT,
PORTON, NEAR SALISBURY, WILTS.

[*Received, April 25th,* 1956.]

[25] Aldridge, *Analyst*, 1944, **69**, 262; 1945, **70**, 474.

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## 757. *Antituberculosis Agents. Part II.*[1] *Dehydrobromination Products and Related Bases derived from Bis-2 : 3-dibromopropyl Sulphide*

By D. EDWARDS and J. B. STENLAKE.

Monodehydrobromination of bis-2 : 3-dibromopropyl sulphide yields 2 : 3-dibromopropyl 3-bromoprop-2-enyl sulphide (II). Further dehydrobromination gives a mixture of bis-3-bromoprop-2-enyl sulphide (VII) and 2-bromoprop-2-enyl 3-bromoprop-2-enyl sulphide (VIII), from which the former may be isolated after the latter has reacted with diethylamine to yield 3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphide (IX). The influence of substituents on the relative reactivity of vinylic bromides is discussed, and it is shown that whereas bis-3-bromoprop-2-enyl sulphide (VII) undergoes rapid solvolysis in 90% acetic acid, the corresponding sulphone is stable under these conditions. Oxidation of the sulphides (VII) and (VIII) with hydrogen peroxide in acetic acid is accompanied by rearrangement, which is demonstrated by the isolation of basic derivatives on subsequent reaction with diethylamine.

BISDIALKYLAMINOALKYL SULPHIDES of varying chain length are more active than the corresponding sulphones against *M. tuberculosis in vitro*,[1] activity increasing with the chain length. Unsaturation enhances activity so that bis-3-diethylaminoprop-1-enyl sulphone

[1] Part I, Edwards and Stenlake, *J. Pharm. Pharmacol.*, 1955, **7**, 852.

is nearly the equal of bis-10-diethylaminodecyl sulphone, the most active of the saturated sulphones examined. The present investigation arose out of an attempt to prepare bis-3-diethylaminoprop-1-enyl sulphide and related unsaturated sulphides for examination.

Bis-3-diethylaminoprop-1-enyl sulphone was prepared from diallyl sulphone by addition of bromine, followed by dehydrobromination, to give bis-3-bromoprop-1-enyl sulphone which was condensed with diethylamine.[1] An analogous route from diallyl sulphide was therefore considered. Rothstein [2] has shown that 2-bromo-1 : 1-diethylthiopropane, $CH_3CHBr{\cdot}CH(SEt)_2$, is readily dehydrobrominated to 1 : 1-diethylthiopropene, $CH_3{\cdot}CH{:}CH(SEt)_2$, in accordance with the Saytzeff elimination rule. However, application of the rule to the proposed dehydrobromination of bis-2 : 3-dibromopropyl sulphide gave no indication as to the direction in which elimination might be expected, although by analogy with the corresponding sulphone αβ-elimination seemed probable.

Bis-2 : 3-dibromopropyl sulphide (I) was readily obtained from allyl sulphide,[3] but attempts to remove hydrogen bromide from it with pyridine failed. It appears, therefore, that electron accession from the lone pairs on the adjacent sulphide link inhibits attack at the α-position, these being conditions which do not obtain in the corresponding sulphone where this reaction is smooth. Rothstein [4] has shown similarly that, whilst benzyl 2-chloropropyl sulphone undergoes smooth dehydrobromination in pyridine, the isomeric benzyl 3-chloropropyl sulphone, which because of the more remote sulphone group is not activated for elimination, resists the attack. On the other hand, stronger bases such as potassium hydroxide in aqueous or absolute ethanol, readily removed acid from bis-2 : 3-dibromopropyl sulphide, the first experiment giving a tribromo-sulphide and a mixture of dibromo-sulphides (A); control of the conditions afforded only the dibromo-sulphides (A).

Ozonolysis of the tribromo-sulphide gave minute amounts of formaldehyde, but hydrobromic acid in almost theoretical yield, indicating its structure as (II). The dehydrobromination is thus analogous to that of αβ-dibromo*iso*butyraldehyde diethyl acetal (IV), which yields β-bromo-α-methylacraldehyde diethyl acetal (V) by βγ-elimination. The small

$$\underset{\text{(IV)}}{CH_2Br{\cdot}CBrMe{\cdot}CH(OEt)_2} \longrightarrow \underset{\text{(V)}}{CHBr{:}CMe{\cdot}CH(OEt)_2} \longrightarrow \underset{\text{(VI)}}{NHPh{\cdot}CH{:}CMe{\cdot}CH{:}NPh}$$

yield of formaldehyde was probably due to contamination by traces of the isomeric sulphide (III), rather than to anomalous ozonolysis,[6,7] since although the latter has been observed with 4-ethoxybut-2-ene, bis-3-bromoprop-2-enyl sulphide (VII) gives no formaldehyde. Formation of some tribromide (III), albeit in low yield, suggested that the dibromo-sulphides (A) contained the isomers (VII) and (VIII). Distillation failed to separate them, but their presence was established by ozonolysis, by isolation of bis-3-bromoprop-2-enyl sulphide (VII), and by the reactions of the base derived from 3-bromoprop-2-enyl 2-bromoprop-2-enyl sulphide (VIII) and diethylamine.

The dibromo-sulphides (A) reacted only slowly with boiling diethylamine, giving a monoacid base, $C_{10}H_{18}SNBr$ : bis-3-bromoprop-2-enyl sulphide (VII) was unaffected and was recovered. The latter also failed to react with hot diethylamine, in benzene or alone under pressure. The base similarly failed to react further with diethylamine. The non-reactivity of the bromo-substituents in these two substances agrees with their formulation as vinylic halides.

The structure of bis-3-bromoprop-2-enyl sulphide (VII) was confirmed by ozonolysis, which gave no formaldehyde but liberated 1·70 mols. of hydrobromic acid. Ozonolysis of the mixed dibromo-sulphides (A), on the other hand, gave 0·19 mol. of formaldehyde [0·29 mol. after allowance for the presence of (VII)], in agreement with structure (VIII)

[1] Rothstein, *J.*, 1940, 1553.
[2] McKitterick, *Ind. Eng. Chem.*, 1929, **21**, 585.
[3] Rothstein, *J.*, 1934, 684.
[4] Hamer and Rathbone, *J.*, 1945, 595.
[6] Knights and Waight, *J.*, 1955, 2830.
[7] Young, McKinnis, Webb, and Roberts, *J. Amer. Chem. Soc.*, 1946, **68**, 293.

for the second component : the alternative structure, $CHBr{:}CH{\cdot}CH_2{\cdot}S{\cdot}CHBr{\cdot}CH{:}CH_2$, for this component was rejected since its formation would require rearrangement which was considered unlikely under the alkaline conditions of the dehydrobromination.[8,9]

Adoption of structures (VII) and (VIII) leads to an assignment of structure (IX) to the base $C_{10}H_{18}SNBr$ derived from the latter. Retention of the vinylidene group in this base was confirmed by liberation of formaldehyde on ozonolysis : the low yield (0·13 mol.) is attributed to the small scale of the reaction, comparably small yields being obtained under similar conditions with test compounds of known structure. Oxidation with hydrogen peroxide gave the sulphone (X), which similarly on ozonolysis gave hydrobromic acid and formaldehyde (0·12 mol.). Formation of a base by reaction of a vinylic halide with diethylamine at first sight seemed improbable ;[10] there is some evidence, however, that suitably substituted vinylic bromides are more reactive than the corresponding chlorides, presumably owing to the greater polarisability of the bromine. For example, Hamer and Rathbone [5] have shown that β-bromo-α-methylacraldehyde diethyl acetal (V) readily gives β-anilino-α-methylacraldehyde anil (VI). On the other hand Parcell and Pollard [11] found that only the allylic bromine atom of 2 : 3-dibromopropene was replaced in reaction with diethylamine. Other replacement reactions which appear to be general to allylic bromides are the formation of lithium alkenyls [12] and replacement by metal alkoxides [13] or thioalkoxides.[14] We have now found that bis-3-bromoprop-2-enyl sulphide undergoes almost complete solvolysis in 90% acetic acid, hydrobromic acid being liberated in 91% of the theoretical yield after 1 hour's refluxing. The product, 3-acetoxyprop-2-enyl sulphide (XI), was unstable and could not be fully characterised. Reactivity in vinylic bromides, however, is not completely general, being governed by the nature of adjacent substituents. For example, Dufraisse and Netter [15] found that only the ethoxygroup of α-bromo-β-ethoxybenzylidene acetophenone reacts with piperidine. Similarly, we have found that bis-3-bromoprop-2-enyl sulphone, unlike the sulphide, does not undergo solvolysis in boiling 90% acetic acid : replacement of an electron-denoting (sulphide) group by an electron-attracting (sulphone) substituent in the 1-position exerts a profound effect on the reactivity of the halogen atom in the 3-bromoprop-2-enyl residue. The difference in reactivity of the bromo-substituents in 2-bromoprop-2-enyl 3-bromoprop-2-enyl sulphide (VIII) can be explained in the same way by the proximity of the methylenethio-group, $-S{\cdot}CH_2-$, to the vinylic halogen of the 2-bromoprop-2-enyl fragment so that substitution with diethylamine occurs in the 2-position, with the formation of 3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphide (IX).

Oxidation of the dehydrobromination product (A) with hydrogen peroxide in acetic acid gave an oil, which, contrary to expectation, reacted with diethylamine, permitting separation into basic and non-basic fractions. The base, $C_{10}H_{18}O_2NBrS$, was not identical with (X) and is formulated as 2-bromoprop-2-enyl 1-diethylaminoprop-2-enyl sulphone (XIII), being derived from 1-bromoprop-2-enyl 2-bromoprop-2-enyl sulphone (XII), which is formed by the thiotropic rearrangement and oxidation of the sulphide (VIII). Rothstein [8] has reported that oxidation of the thioacetal, $CH_2{:}CH{\cdot}CH(SEt)_2$, is accompanied by migration of an ethylthio-group to yield 1 : 3-diethylsulphonylpropene. A similar rearrangement of vinylic to allylic bromide is supported in the present case by the ease with which the rearranged and oxidised product reacted with diethylamine. Reaction was instantaneous at room temperature, and comparable in ease with that between bis-3-bromoprop-1-enyl sulphone and diethylamine. Ozonolysis of the sulphone (XII) was not completely satisfactory owing to the small amount of material available. Formaldehyde was obtained but in only 8% of the theoretical yield for two vinylidene groups, although this yield is comparable on a weight basis with those obtained from the sulphides (IX) and

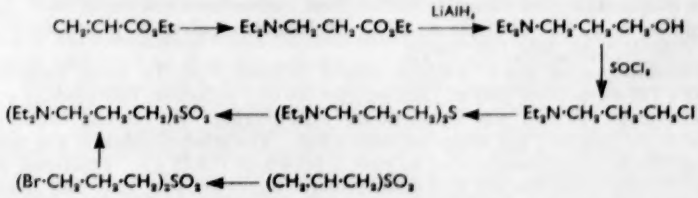
[8] Rothstein, *J.*, 1940, 1560.
[9] Jones and Weedon, *J.*, 1946, 937.
[10] Ingold and Rothstein, *J.*, 1929, 8.
[11] Parcell and Pollard, *J. Amer. Chem. Soc.*, 1950, **72**, 2385.
[12] Braude and Timmons, *J.*, 1950, 2000.
[13] Winstein, Lindegren, and Ingraham, *J. Amer. Chem. Soc.*, 1953, **75**, 155.
[14] Laevenich, Losen, and Dierichs, *Ber.*, 1927, **60**, 950.
[15] Dufrasse and Netter, *Bull. Soc. chim. France*, 1932, **51**, 550.

(X). Hydrobromic acid was also obtained, indicating the retention of one vinylic bromine in the molecule.

The oily non-basic substance obtained on oxidation of the dibromo-sulphides (A), isolated after reaction with diethylamine, was separated by distillation into two fractions. One was bis-3-bromoprop-2-enyl sulphone (XIV), identical with the principal oxidation product of bis-3-bromoprop-2-enyl sulphide (VII). Its structure was confirmed by its failure to react with diethylamine, and the absence of formaldehyde and liberation of hydrobromic acid (1·66 mol.) on oxonolysis. The higher-boiling fraction afforded a material, $C_{10}H_{19}O_2BrS$, from which ozonolysis yielded hydrobromic acid but no formaldehyde, indicating the presence of an intact $CHBr{:}CH{\cdot}CH_2{\cdot}SO_2$ group in the molecule.

Oxidation of bis-3-bromoprop-2-enyl sulphide (VII) was accompanied by partial rearrangement to 1-bromoprop-2-enyl 3-bromoprop-2-enyl sulphone (XV), since the oily product reacted with cold diethylamine (indicative of an allyl bromide group) to give small yields of a monoacid base, insufficient for characterisation but presumably 3-bromoprop-2-enyl 1-diethylaminoprop-2-enyl sulphone (XVI); crystalline bis-3-bromoprop-2-enyl sulphone (XIV) was also isolated. In an experiment on a larger scale the crude base from the oxidation of the dibromo-sulphides (A) gave low equivalent weights, suggesting the presence of a diacidic base, tentatively formulated as bis-1-diethylaminoprop-2-enyl sulphone. The latter, like bis-3-diethylaminoprop-1-enyl sulphone, decomposed on distillation of the crude product, but small amounts were isolated from the undistilled material as the crystalline dihydrochloride, the melting point of which was depressed on admixture with bis-3-diethylaminoprop-1-enyl sulphone dihydrochloride.

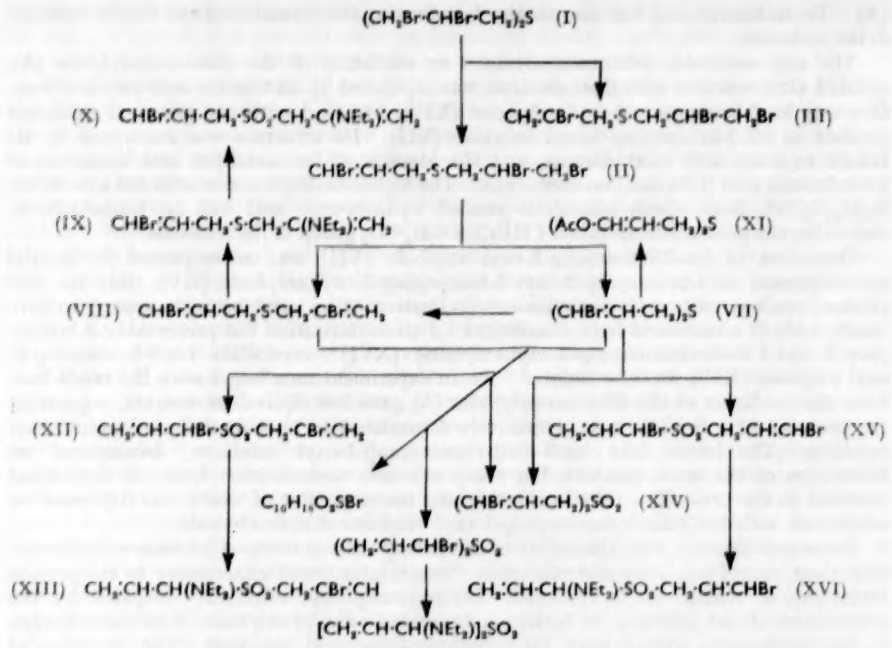
Some experiments, with the object of comparing the reactivity of 3-bromo-substituents in various propyl sulphides and sulphones, though later found unnecessary to the present investigation, remain to be recorded. Bis-3-bromopropyl sulphone,[1] prepared by the peroxide-catalysed addition of hydrogen bromide to diallyl sulphone, with diethylamine in boiling benzene slowly gave bis-3-diethylaminopropyl sulphone. The direction of addition of hydrogen bromide, and hence the 3-position of the bromo-substituent, have now been confirmed by the preparation of bis-3-diethylaminopropyl sulphone from bis-3-diethylaminopropyl sulphide,[16] which we obtained by the following annexed routes:




Peroxide-catalysed addition of hydrobromic acid to allyl sulphide under the conditions used for addition to the corresponding sulphone, gave bis-2-bromopropyl sulphide, and not the expected bis-3-bromopropyl sulphide. This was confirmed by its reaction with diethylamine, which was extremely slow in benzene, to give a diacidic base bis-2-diethylaminopropyl sulphide, the hydrochloride of which depressed the melting point of bis-3-diethylaminopropyl sulphide. It is conceivable that the sulphide link could offset the influence of peroxide on the course of hydrogen bromide addition, the peroxide being eliminated in an oxidation of the sulphide group. This, however, is in direct contradiction to Jones and Reid's demonstration [17] of the catalytic effects of even traces of peroxides on the course of addition of thiols to unsaturated compounds.

An attempt to prepare bis-3-bromopropyl sulphide by a controlled reaction between 1 : 3-dibromopropane and sodium sulphide gave only a small yield of a bis-3-bromopropyl tetrasulphide, which was characterised by conversion into bis-3-diethylaminopropyl tetrasulphide dihydrochloride.

[16] Andrews, Bergel, and Morrison, *J.*, 1953, 2998.
[17] Jones and Reid, *J. Amer. Chem. Soc.*, 1938, **60**, 2452; *Org. Synth.*, Coll. Vol. I, 1st. edn., p. 23.




## Experimental

*Bis-2 : 3-dibromopropyl Sulphide.*—Diallyl sulphide (14·33 g.) was slowly treated in carbon tetrachloride (100 ml.) with bromine (41 g.) in carbon tetrachloride (30 ml.). The residue obtained on evaporation gave colourless needles (from carbon tetrachloride) of bis-2 : 3-dibromopropyl sulphide, m. p. 92—93·5° (31 g., 57%) (McKitterick [3] gives m. p. 94—95·5°) (Found : Br, 73·9. Calc. for $C_6H_{10}SBr_4$ : Br, 73·7%).

*Dehydrobromination of Bis-2 : 3-dibromopropyl Sulphide.*—(*a*) To bis-2 : 3-dibromopropyl sulphide (15 g.) in warm ether (100 ml.) and ethanol (40 ml.) potassium hydroxide (4 g.) in water (3 ml.) and ethanol (20 ml.) was added slowly with stirring. On cooling, the mixture was poured into water (400 ml.) and extracted with ether. The ethereal solution was washed with water, dried ($Na_2SO_4$), and evaporated to yield a brown oil (10·22 g.). Fractional distillation of a portion (8·13 g.) gave fraction A, a straw-coloured liquid (A), b. p. 125—130° (bath)/4 mm., $n_D^{19}$ 1·5990 (3·6 g.) (1·5979 after redistillation) (Found: Br, 58·5. Calc. for $C_6H_8SBr_2$: Br, 58·8%), and B, *3-bromoprop-2-enyl 2 : 3-dibromopropyl sulphide*, a yellow liquid, b. p. 118—119°/0·75 mm., $n_D^{18}$ 1·6125 (3·5 g.) (Found : Br, 69·3. $C_6H_8SBr_3$ requires Br, 67·9%).

(*b*) Bis-2 : 3-dibromopropyl sulphide (11·75 g.) in benzene (50 ml.) and ethanol (20 ml.) was treated with potassium hydroxide (3·1 g.) in ethanol (60 ml.) slowly with stirring. After 10 minutes' stirring, the potassium bromide was filtered off and the bulk of the solvent removed. The residual liquid was poured into water (120 ml.) and extracted with benzene. The benzene solution, after drying ($Na_2SO_4$) and evaporation, gave the mixture (A) of bis-3-bromoprop-2-enyl sulphide and 3-bromoprop-2-enyl 2-bromoprop-2-enyl sulphide ($n_D^{20}$ 1·5942; 7·09 g., 95%), obtained after distillation as a straw-coloured liquid, b. p. 96—97°/1·3 mm., $n_D^{28}$ 1·5961.

*Ozonolysis of the Mixed Dibromo-sulphides (A).*—The mixture (A) (1·022 g.) was ozonised in chloroform (25 ml.) for 1 hr. The solvent was removed under pressure, and the oily product hydrolysed by refluxing with water (40 ml.) for 30 min. Steam-distillation and treatment of the distillate with dimedone yielded the formaldehyde–dimedone derivative (0·211 g., 0·193 mol.). Treatment of the aqueous solution, remaining after steam-distillation, with nitric acid (1 ml.) and an excess of silver nitrate solution gave silver bromide (0·92 g., 1·3 mols.).

*Ozonolysis of 3-Bromoprop-2-enyl 2 : 3-Dibromopropyl Sulphide.*—3-Bromoprop-2-enyl 2 : 3-dibromopropyl sulphide (0·944 g.) was ozonised in chloroform as described above, and yielded

the formaldehyde–dimedone derivative (0·023 g., 0·29 mol.) and hydrobromic acid (as silver bromide, 0·502 g., 0·92 mol.).

*Reaction of the Mixed Dibromo-sulphides (A) with Diethylamine.*—The mixture (A) (9·5 g.) in benzene (120 ml.) was refluxed with diethylamine (25 ml.) for 1 hr. Excess of diethylamine and benzene were removed by distillation, and the residue washed in benzene with water and extracted with dilute hydrochloric acid. The aqueous solution was made alkaline with sodium hydroxide solution, and the liberated base extracted with benzene. This benzene solution was washed with water, dried ($Na_2SO_4$), and evaporated to a yellow liquid (5·42 g.) which on distillation gave *3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphide*, b. p. 123—128° (bath)/3·5 mm., $n_D^{19}$ 1·5300 (Found: N, 5·2%; equiv., 263·6. $C_{10}H_{18}NSBr$ requires N, 5·3%; equiv., 264·2).

The benzene solution remaining after extraction with hydrochloric acid was washed with water, dried ($Na_2SO_4$), and evaporated under reduced pressure to a liquid (2·69 g.) which on distillation gave *bis-3-bromoprop-2-enyl sulphide* as a pale straw-coloured liquid, b. p. 120—125° (bath)/3·5 mm., $n_D^{20}$ 1·5958 (Found: C, 26·5; H, 3·15. $C_6H_8SBr_2$ requires C, 26·5; H, 3·0%).

*Ozonolysis of 3-Bromoprop-2-enyl 2-Diethylaminoprop-2-enyl Sulphide.*—This sulphide (0·679 g.), ozonised as described above, yielded the formaldehyde–dimedone derivative (0·0979 g., 0·13 mol.) and hydrobromic acid (not estimated).

*Ozonolysis of Bis-3-bromoprop-2-enyl Sulphide.*—The sulphide (0·962 g.), ozonised as above, gave only a trace of formaldehyde–dimedone derivative. Treatment of the aqueous solution remaining after steam-distillation with nitric acid (1 ml.) and silver nitrate, gave silver bromide (1·125 g., 1·69 mols.).

*Attempts to Condense Bis-3-bromoprop-2-enyl Sulphide with Diethylamine.*—(*a*) The sulphide (1 g.) in benzene (20 ml.) was refluxed with diethylamine (2·5 ml.) for 2 hr., and the mixture left at room temperature overnight, then evaporated to dryness and dissolved in benzene, washed with water, and extracted with dilute hydrochloric acid. The residual solution was washed, dried ($Na_2SO_4$), and evaporated, to yield unchanged bis-3-bromoprop-2-enyl sulphide (0·93 g.), $n_D^{20}$ 1·5959. The acid aqueous extract was made alkaline with sodium hydroxide solution and extracted with benzene. The benzene solution was washed, dried ($Na_2SO_4$), and evaporated, to yield a trace of a reddish base, $n_D^{22·5}$ 1·5262, insufficient for characterisation.

(*b*) Bis-3-bromoprop-2-enyl sulphide (3·63 g.) was heated with diethylamine (6 ml.) at 130—140° for 2·5 hr. in a steel bomb (40 ml. capacity). On cooling and extraction as above unchanged sulphide (3·45 g.), $n_D^{20}$ 1·5956, was obtained, together with traces of a base, $n_D^{20}$ 1·5278.

*Reaction of Bis-3-bromoprop-2-enyl Sulphide with 90% Acetic Acid.*—The sulphide (1·093 g.) was heated at 100° for 1 hr. in acetic acid (15 ml.) and water (1·5 ml.). The solution became dark red. After dilution with water (60 ml.) and partial neutralisation with sodium hydroxide the then cloudy solution was extracted with benzene. The benzene solution was washed with water, dried ($Na_2SO_4$), and evaporated to yield a liquid (0·75 g.) which distilled with considerable decomposition, yielding a pale yellow oil (0·266 g.), b. p. 95—100° (bath)/0·35 mm., $n_D^{14}$ 1·5605. The oily product did not restore the colour to Schiff's reagent or reduce ammoniacal silver nitrate solution, but caused immediate reduction of Tollens's reagent. Sodium hydroxide solution elicited a pleasant odour, but the solution rapidly resinified. The product was unstable and decomposed rapidly, so that analytical figures could not be obtained. The residual aqueous liquid from the benzene extraction, on addition of nitric acid and excess of silver nitrate, gave silver bromide (1·369 g., 1·81 mols.).

*3-Bromoprop-2-enyl 2-Diethylaminoprop-2-enyl Sulphone.*—3-Bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphide (1 g.) was treated in glacial acetic acid (15 ml.) at 5° with 30% hydrogen peroxide (3 ml.) and set aside overnight at room temperature. The solution was then heated to 80—85° for 1 hr., cooled, and diluted with water (50 ml.). A slight excess of sodium hydroxide solution was added, and the liberated base extracted with benzene. The benzene extracts were washed, dried ($Na_2SO_4$), and evaporated under reduced pressure, to yield *3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphone*, b. p. 140° (bath)/1·4 mm., $n_D^{18·5}$ 1·5343, $d^{19}$ 1·284 (0·32 g., 29·2%) (Found: N, 4·6%; equiv., 294·3. $C_{10}H_{18}O_2NBrS$ requires N, 4·7%; equiv., 296·2).

This sulphone (0·27 g.) was ozonised in chloroform, and the ozonide hydrolysed to yield formaldehyde, isolated as the dimedone derivative (0·033 g., 0·124 mol.), and hydrobromic acid (not estimated).

*Oxidation of the Mixed Dibromo-sulphides (A).*—The dibromo-sulphides (A) (5·614 g.) were oxidised in acetic acid (70 ml.) with 30% hydrogen peroxide (14 ml.), as above. The mixture

was poured into water (300 ml.) and extracted with benzene. Evaporation of the benzene solution gave a yellow oil (5·467 g.), $n_D^{24\cdot6}$ 1·5683, subsequently shown to be a mixture of bis-3-bromoprop-2-enyl sulphone, 1-bromoprop-2-enyl 2-bromoprop-2-enyl sulphone, bis-1-bromoprop-2-enyl sulphone, and a substance $C_{10}H_{19}O_2BrS$.

*Reaction of the Mixed Dibromo-sulphones with Diethylamine.*—The mixed product from the above reaction (5·45 g.) in benzene (50 ml.) was treated with diethylamine (7 ml.) and heated on a water-bath for 5 min. to complete the reaction (apparently instantaneous). After removal of the solvent under reduced pressure, the residue was washed with water and extracted with benzene. The benzene solution was extracted with dilute hydrochloric acid, and the acid solution basified with aqueous sodium hydroxide and extracted with benzene, to give an oily base (2·296 g.), $n_D^{14}$ 1·5110 (Found : equiv., 247·6. Calc. for $C_{14}H_{28}O_2N_2S$ : equiv., 144·2. Calc. for $C_{10}H_{18}O_2NSBr$ : equiv., 296·2). The crude mixed bases (1·131 g.) were distilled with considerable decomposition, to yield *2-bromoprop-2-enyl 1-diethylaminoprop-2-enyl sulphone* as a yellow oil (0·453 g.), b. p. 170—175° (bath)/1·7 mm., $n_D^{14}$ 1·5158, $d^{19}$ 1·307 (Found : N, 4·9%; equiv., 295·3. $C_{10}H_{18}O_2NBrS$ requires N, 4·7%; equiv., 296·2). The crude mixed bases (0·2 g.) were dissolved in dilute hydrochloric acid and carefully evaporated. The residue (from ethanol–ether) gave a small yield of colourless bis-1-diethylaminoprop-2-enyl sulphone dihydrochloride, m. p. 189—190° (insufficient for analysis), mixed m. p. with bis-3-diethylaminoprop-1-enyl sulphone hydrochloride (m. p. 192—193°) 176—179°.

Non-basic oxidation products were obtained by evaporation of the benzene solution remaining after the extraction of bases with hydrochloric acid as a reddish-brown oil (2·24 g.), $n_D^{14}$ 1·5624, containing some crystals. Distillation yielded fractions A and B. Fraction A was a yellowish liquid (1·2 g.), b. p. 160—165° (bath)/1·3 mm., which solidified. The solid was separated from traces of oil by chromatography from ether on alumina. The crystalline product isolated from the first fraction of the eluate gave [from light petroleum (b. p. 40—60°)] colourless plates of *bis-3-bromoprop-2-enyl sulphone*, m. p. 65·5—66·5° (Found : C, 23·8; H, 3·0; Br, 52·15. $C_6H_8O_2Br_2S$ requires C, 23·7; H, 2·7; Br, 52·6%). Fraction B was a yellow oil (1·5 g.), b. p. 180—200° (bath)/1·3 mm., which solidified to yield a *bromo-compound* as colourless prisms (from ether), m. p. 73—74° (Found : C, 42·95, 41·9; H, 6·3, 6·5; Br, 28·1. $C_{10}H_{19}O_2SBr$ requires C, 42·4; H, 6·8; Br, 28·2%).

*Ozonolysis of 2-Bromo-2-enyl 1-Diethylaminoprop-2-enyl Sulphone.*—This sulphone (0·247 g.), ozonised in chloroform, gave formaldehyde, isolated as the dimedone derivative (0·039 g., 0·158 mol.) and hydrobromic acid (not estimated).

*Ozonolysis of Bis-2-bromoprop-2-enyl Sulphone.*—The sulphone (0·413 g.), ozonised in chloroform, yielded only a trace of formaldehyde. Treatment of the aqueous solution, remaining after steam-distillation, with nitric acid (1 ml.) and excess of silver nitrate gave silver bromide (0·421 g., 1·63 mol.).

*Ozonolysis of the Neutral Compound,* $C_{10}H_{19}O_2BrS$.—This compound (0·289 g.) gave no formaldehyde, but gave hydrobromic acid in good yield (not estimated).

*Oxidation of Bis-3-bromoprop-2-enyl Sulphide and Reaction of the Products with Diethylamine.*—Bis-3-bromoprop-2-enyl sulphide (2·33 g.) in acetic acid (30 ml.) was oxidised with 30% hydrogen peroxide (5·5 ml.) as described in the preparation of 3-bromoprop-2-enyl 2-diethylaminoprop-2-enyl sulphone. The resulting solution was poured into water (150 ml.) and extracted with benzene. The benzene solution was washed, dried ($Na_2SO_4$), and evaporated under reduced pressure to a yellow oil (2·45 g.), which partly crystallised. The oil was dissolved in benzene (20 ml.), warmed with diethylamine (2·5 ml.) for 5 min., evaporated to dryness, and extracted with benzene. Separation of basic and non-basic products by benzene and dilute acid as before gave a basic fraction, probably *3-bromoprop-2-enyl 1-diethylaminoprop-2-enyl sulphone*, a reddish-brown oil (0·117 g.), $n_D^{14}$ 1·5123 (Found : equiv., 293·3. $C_{10}H_{18}O_2NBrS$ requires equiv., 296·2), and a non-basic yellow oil (2·091 g.), $n_D^{14}$ 1·5649, which gave, on distillation, a colourless oil (1·75 g.), b. p. 145—150° (bath)/0·6 mm., which solidified and when chromatographed from ether on alumina and recrystallised from light petroleum gave colourless plates of bis-3-bromoprop-2-enyl sulphone, m. p. and mixed m. p. 65·5—66·5°.

*Attempted Solvolysis of Bis-3-bromoprop-2-enyl Sulphone.*—The sulphone (1·38 g.) was heated with acetic acid (19 ml.) and water (2 ml.) for 1·25 hr. on a boiling-water bath, cooled, poured into water (150 ml.), and extracted with benzene. Evaporation of the benzene gave unchanged bis-3-bromoprop-2-enyl sulphone (1·232 g.), m. p. and mixed m. p. 65·5—66·5°.

*Other Materials.*—Ethyl 3-diethylaminopropionate, prepared by Adamson's method,[18] had b. p. 87°/15 mm., $n_D^{17\cdot5}$ 1·4290. Adamson reports b. p. 87—88°/15 mm.

[18] Adamson, *J.*, 1949, S 144.

Diethyl-3-hydroxypropylamine, prepared by lithium aluminium hydride reduction of ethyl β-diethylaminopropionate (82 g.), had b. p. 81°/15 mm., $n_D^{17.5}$ 1·4430 (50·8 g., 81·8%). Von Braun [19] reports b. p. 84°/20 mm.

*3-Chloropropyldiethylamine.* Thionyl chloride (37 ml.) in benzene (90 ml.) was slowly added to a solution of diethyl-3-hydroxypropylamine (50·8 g.) in benzene (250 ml.). The solvent was removed under reduced pressure to yield a brown crystalline mass. The product was dissolved in water (60 ml.), cooled to 0°, basified by 20% sodium hydroxide solution (85 ml.), and extracted with ether. The ethereal solution was washed, dried ($Na_2SO_4$), and evaporated, and the residual oil distilled to give 3-chloropropyldiethylamine, b. p. 62—65°/16 mm., $n_D^{20}$ 1·4417 (49·22 g., 84·9%) (lit.,[20] b. p. 53—57°/12 mm.).

*Bis-3-diethylaminopropyl sulphide.* 3-Chloropropyldiethylamine (36·51 g.) in ethanol (24 ml.) was slowly added to a hot solution of anhydrous sodium sulphide (13 g.) in water (14 ml.) and ethanol (35 ml.), and the mixture was refluxed for 3·5 hr. with continuous stirring. The residual liquor, after removal of the bulk of the ethanol by distillation, was poured into water (350 ml.), and extracted with ether. The ethanol solution was washed, dried ($Na_2SO_4$), and evaporated. Fractional distillation of the residual oil gave a forerun of unchanged 3-chloropropyldiethylamine followed by bis-3-diethylaminopropyl sulphide, b. p. 133—136°/2·5 mm., $n_D^{18}$ 1·4758 (21·71 g., 68·4%). Andrews, Bergel, and Morrison [16] gave b. p. 80—81°/0·03 mm., $n_D^{21}$ 1·4731 (Found: equiv., 131·1. Calc. for $C_{14}H_{32}N_2S$: equiv., 130). Its *dihydrochloride* (from ethanol) has m. p. 222·5—223·5° (Found: N, 8·5; Cl, 21·4. $C_{14}H_{34}N_2Cl_2S$ requires N, 8·4; Cl, 21·3%).

*Bis-3-diethylaminopropyl sulphone.* Potassium permanganate (3%) in acetic acid (50%) was added during 20 min. to an ice-cold solution of bisdiethylaminopropyl sulphide (3·5 g.) in 50% acetic acid (6 ml.) until present in slight excess. After a further 20 min. the solution was decolorised with sulphur dioxide and evaporated to dryness under reduced pressure. Sodium carbonate solution was added to alkalinity, and the solution again evaporated to dryness. The solid residue, on continuous extraction with ether, removal of solvent, and distillation, gave *bis-3-diethylaminopropyl sulphone*, b. p. 186°/3·5 mm., $n_D^{24.5}$ 1·4707 (3·5 g., 90%) (Found: C, 57·75; H, 10·8; N, 9·5. $C_{14}H_{32}O_2N_2S$ requires C, 57·5; H, 11·0; N, 9·6%). Its dihydrochloride had m. p. 186·5—187°, mixed m. p. with bis-3-diethylaminopropyl sulphone dihydrochloride 186·5—187°.

*Addition of Hydrogen Bromide to Diallyl Sulphide.*—Diallyl sulphide (7·27 g.) was dissloved in carbon tetrachloride (100 ml.). A crystal of benzoyl peroxide was added, the solution heated to the b. p., and dry hydrogen bromide passed in whilst the solution was cooling and thereafter for 22 hr. The solution was brought to the b. p. at 3-hourly intervals, being allowed to cool to room temperature during the intervening periods. Evaporation of the solvent under reduced pressure gave a yellow liquid (13·7 g.), which yielded on distillation *2-bromopropyl prop-2-enyl sulphide*, b. p. 49—50°/1·7 mm., $n_D^{17.5}$ 1·5275 (5·5 g.) (Found: Br, 41·8. $C_6H_{11}BrS$ requires Br, 41·0%), and *bis-2-bromopropyl sulphide*, b. p. 95°/0·95 mm., $n_D^{19}$ 1·5547 (7·1 g.) (Found: Br, 58·3. $C_6H_{12}Br_2S$ requires Br, 58·0%).

*Bis-2-diethylaminopropyl Sulphide.*—Bis-2-bromopropyl sulphide (1·042 g.) in benzene (12 ml.) was refluxed with diethylamine (2 ml.) for 5 hr. The basic product, extracted in the usual way as a yellow oil (0·461 g.), b. p. 80°/1·2 mm., $n_D^{18}$ 1·4747 (Found: equiv., 142·3. $C_{14}H_{32}N_2S$ requires equiv., 130·1), was treated with dilute hydrochloric acid, to give *bis-2-diethylaminopropyl sulphide dihydrochloride*, m. p. 224—226° (decomp.) (from ethanol–ether) (Found: N, 8·45; Cl, 21·3. $C_{14}H_{34}N_2Cl_2S$ requires N, 8·4; Cl, 21·3%). A mixed m. p. with bis-3-diethylaminopropyl sulphide dihydrochloride (m. p. 222·5—223·5°) was depressed to 211—212·5°.

*Bis-3-bromopropyl Tetrasulphide.*—1 : 3-Dibromopropane (40·4 g.) [17] was added to a stirred solution of sodium sulphide (7·8 g.) in water (10 ml.) and ethanol (45 ml.). The mixture was refluxed for 3·5 hr., cooled, poured into water (250 ml.), and extracted with benzene. The benzene solution was washed with water, dried ($Na_2SO_4$), and evaporated under reduced pressure, to a brown oil, which on distillation gave *bis-3-bromopropyl tetrasulphide* as a pale yellow oil (6·32 g., 17%), b. p. 121—125°/1·2 mm., $n_D^{13}$ 1·5538 (Found: 42·4. $C_6H_{12}Br_2S_4$ requires Br, 42·9%).

*Bis-3-diethylaminopropyl Tetrasulphide Dihydrochloride.*—Bis-3-bromopropyl tetrasulphide (2·31 g.) in benzene (20 ml.) was refluxed with diethylamine (4 ml.) for 1·5 hr. The basic product was extracted in the usual way as a yellow oil (1·34 g.), which on distillation gave a

[19] Von Braun, *Ber.*, 1916, **49**, 966.
[20] Von Marxer, *Helv. Chim. Acta*, 1941, **24**, 209E.

colourless oil, b. p. 155—160° (bath)/1·6 mm., $n_D^{17\cdot4}$ 1·4988. This gave *bis-3-diethylaminopropyl tetrasulphide dihydrochloride*, needles, m. p. 245·5—246·5° (from ethanol) (Found: C, 39·8; H, 7·5; N, 6·7; Cl, 17·0. $C_{14}H_{34}N_2Cl_2S_4$ requires C, 39·1; H, 8·0; N, 6·5; Cl, 16·5%).

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## 758. *The Rates of Reaction of Copper, Zinc, and Uranium with Organic Solvent–Dinitrogen Tetroxide Mixtures.*

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The rate of reaction between metals and liquid dinitrogen tetroxide is increased considerably when the tetroxide is mixed with certain organic solvents; this is illustrated by measurements with copper, zinc, and uranium. Solvents which act as electron-donors (Don) to the tetroxide set up the equilibrium $[(Don)_n.NO^+]NO_3^- \rightleftharpoons n(Don) + N_2O_4 \rightleftharpoons (Don)_n.N_2O_4$, in the liquid state, and the enhanced reaction reflects the increase in concentration of ionic species. Rates of reaction with the oxygen-donor solvents diethyl ether, ethyl acetate, dioxan, and acetic anhydride, the nitrogen-donor solvents phenyl cyanide, benzyl cyanide, methyl cyanide, and diethylnitrosamine, and the non-donor solvent nitromethane are reported over the full liquid concentration range. The variation of reaction rate with concentration has been classified into three types, and each type is interpreted in terms of the dielectric constant of the liquid, the concentration of simple $NO^+$ ions or complex $(Don)_n.NO^+$ ions, the relative powers of the solvent and the $NO_3^-$ ion to act as desorbing agent for the metal cation formed on initial reaction at the metal surface, and the minimum stable valency of the metal. The activation energy of the reactions has been determined. Stirring influences the speed of the reaction, but not its type or activation energy.

THE chemical and physical properties of liquid dinitrogen tetroxide are profoundly modified in the presence of solvents whose molecules can act as electron-pair donors.[1-3] This is attributed to the formation of addition compounds, which may be molecular or ionic in character. The equilibrium in the liquid state between dinitrogen tetroxide and donor solvent (Don) is represented by:

$$[(Don)_n.NO^+]NO_3^- \rightleftharpoons n(Don) + N_2O_4 \rightleftharpoons (Don)_n.N_2O_4$$

Since the ionic and the molecular form of the complex are very different structurally, and since the ionic form can be most easily produced from the molecular form by the dissociation of the latter into its components, we do not consider there to be any direct equilibrium between the ionic and the molecular form of the addition compound. Many of the physical properties of the mixtures (freezing point, viscosity, deviation of vapour pressure from ideality, modification of the absorption spectrum of dinitrogen tetroxide) result from the presence of the molecular complex. It is quite clear from a survey of the properties of the mixtures (including electrical conductivity) that the ionic form of the complex is present in very small proportion, and can often be ignored; it does, however, play the important role in the reaction of these mixtures with metals. Under appropriate conditions the reaction rates with metals reflect the ionic concentration in the medium, but not necessarily the total degree of compound formation. Since there are two electron-deficient species ($NO^+$ and $N_2O_4$), a change in the structure of the solvent may not influence the two equilibria shown above to the same extent, so that a list of solvents drawn up in order of donor strength according to the chemical reactivity of the mixture need not agree precisely with

[1] Addison and Sheldon, *J.*, 1956, 1941.
[2] *Idem*, *J.*, 1956, 2705.
[3] *Idem*, *J.*, 1956, 2709.

one drawn up on the basis of a physical method which takes into account the molecular form of the addition compound also.

This investigation was carried out for two main reasons. First, very few studies of rates of solution of metals in non-aqueous media have been attempted. This is perhaps because diffusion of reactants to (or products from) the surface can play such a predominant rate-determining role as to prevent interpretation of the results in terms of reaction mechanism. In the systems described here, diffusion is less important and it has been possible to define some general features which may be typical of other metal–non-aqueous media reactions. Secondly, many of these reactions result in the formation of new compounds, and a knowledge of the factors controlling reaction rates aids in the selection of new preparative methods. (The products of reaction will be described in later papers.)

Solution rates have been measured for copper, zinc, and uranium. Copper was selected because it has a stable univalent state; zinc because it shows bivalency only, and its rates of reaction with pure dinitrogen tetroxide are known.[4] A limited number of measurements on uranium (carried out by Dr. N. Hodge in this laboratory) are included to show the influence of the higher valency states. Few metals react at a perceptible rate with the pure tetroxide, but mixtures with donor solvents react rapidly with many metals (including cobalt and manganese). Iron, nickel, and chromium and their alloys remain inert, and are thus useful constructional materials in the handling of these mixtures.

*Typical Reaction Rate–Composition Curves.*—These are shown in Fig. 1. Copper does not react with dinitrogen tetroxide or with diethyl ether, yet reaction is vigorous with the mixture, which clearly contains some reactive species. The rates (curve *D*) pass through a very sharp maximum. The position of the peak on the composition axis varies with the donor solvent and does not coincide with any particular $N_2O_4$ : solvent molecular ratio. The zinc curve (*F*) is similar in shape; the rate curve follows that for copper at high tetroxide concentrations (curves *E* and *F*) but the rapid increase in rate with addition of ethyl acetate is arrested sooner. The following experiments were carried out to determine the factors responsible for this unusual behaviour.

*Reaction with Nitromethane Mixtures.*—The $N_2O_4$ molecule ionises into $NO^+$ and $NO_3^-$ in media of high dielectric constant.[5] Before attempting to interpret the rate curves with donor solvents, it is necessary to determine the manner in which metals react with the ionised tetroxide, since the simplest mechanism of reaction involves direct electron transfer from the metal atom to the $NO^+$ ion, with evolution of nitric oxide. Nitromethane ($\varepsilon$ 37) is a suitable solvent for this purpose as it does not form an addition compound with dinitrogen tetroxide.[6] The broken line (Fig. 2) traces the variation in electrical conductivity of the mixtures with composition. The conductivity of the tetroxide increases on addition of nitromethane owing to enhanced ionisation, reaching a maximum near 90 mol.% of nitromethane.[6] Thereafter we may assume that the dielectric constant of the mixture does not change appreciably; the degree of ionisation is not further increased, and the fall in conductivity is due to dilution of the ions. The reaction rate curve for copper with this mixture is of the same form, and its peak coincides with the maximum in the conductivity values on the composition axis. The fastest reaction therefore occurs when the number of $NO^+$ ions is greatest, and the basic reaction is considered to be :

$$Cu + NO^+ \longrightarrow Cu^+ + NO$$

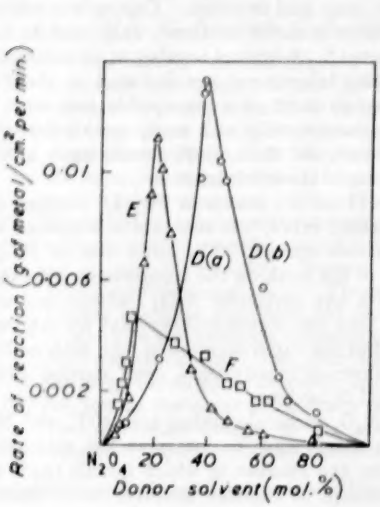
The rate of stirring of the metal in the solution does not alter the shape of the rate curve, or the position of its maximum, but only modifies the actual rate. Since it is therefore of less significance, consideration of the influence of stirring rate is deferred until later in this paper. The simple correlation observed for copper does not hold when the lowest stable valency of the metal exceeds unity. The zinc curve has a shape similar to that for copper, though the maximum is somewhat displaced. The uranium values are magnified in Fig. 2 to show that the maximum in the uranium rate curve bears no relation to the electrical conductivity measurements. In such cases the metal–$NO^+$ reaction is

[4] Addison and Lewis, *J.*, 1951, 2833.
[5] Goulden and Millen, *J.*, 1950, 2620.
[6] Addison, Hodge, and Lewis, *J.*, 1953, 2631.

of a higher order, and the interpretations which follow are applied primarily to copper as representing the simplest case.

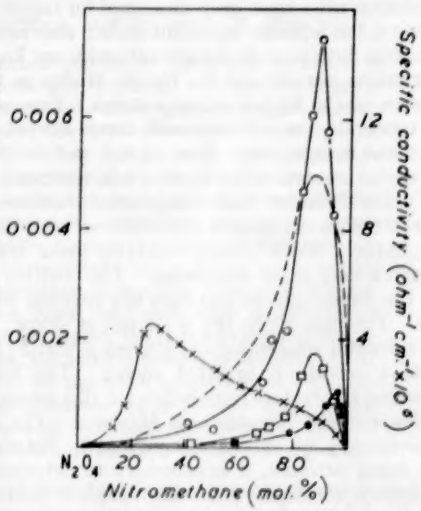
*Classification of Systems.*—The curves obtained are of three distinct types. Type (1) is shown by the curves for copper in Fig. 2, and is the type obtained when the solvent has no appreciable donor properties but a high dielectric constant; it reflects the concentration of $NO^+$ ions in the mixture, so that reaction rates in the 0—50 mol. % concentration range of solvent are often very small indeed. Most electron donor solvents give curves of type (2) (Fig. 1). Addition of such a solvent gives rise immediately to $[(Don)_n.NO^+]NO_3^-$ ion

FIG. 1. *Rates of reaction at 15° and 400 r.p.m.*




| Curve | Metal | Donor solvent |
|---|---|---|
| *D* | Copper | Diethyl ether |
| *E* | Copper | Ethyl acetate |
| *F* | Zinc | Ethyl acetate |

FIG. 2. *Rates of reaction with $N_2O_4$–nitromethane mixtures at 15°.*




—○——○— Copper: stirring rate 400 r.p.m.
—□——□— Copper: unstirred.
—●——●— Zinc: stirring rate 400 r.p.m.
—×——×— Uranium: stirring rate 350 r.p.m. (the uranium rates shown are magnified by a factor of 50).
– – – – – – Electrical conductivity of mixture.

pairs; these increase the dielectric constant of the medium, which leads to separation of the ions, and the rapid increase in reaction rate on addition of small quantities of donor solvent indicates that electron transfer from the metal (M) to the complex, *i.e.*:

$$M + (Don)_n.NO^+ \longrightarrow M^+ + n(Don) + NO$$

is possible with many solvents. The greater the donor strength of the solvent with respect to $NO^+$, the steeper is the initial increase in reaction rate. It might have been expected therefore that reaction rates with donor solvents would greatly exceed those in the presence of non-donor solvents. While this is invariably true at low solvent concentrations, some restrictive effect appears in donor-solvent systems which reduces reaction rate in the 50—100 mol. % solvent-concentration range. The onset of this effect is sudden, giving rise to sharp maxima in the rate curves (Fig. 1, and Figs. 3—5). Most of the solvents studied fall into type (1) or (2). It is of particular interest that a system has been found (copper with methyl cyanide mixtures, Fig. 7) which is of a third type, in which the solvent behaves both as a donor- and an ionising-solvent system.

*Oxygen- and Nitrogen-donors.*—Rate curves for acetic anhydride mixtures are given in

Fig. 3. They are of the same type (1) as is observed for diethyl ether and ethyl acetate (Fig. 1). No inferences should be drawn from the relative magnitudes of the rates with acetic anhydride mixtures and with the other mixtures reported. In all other mixtures the weight of metal dissolved was proportional to the time of immersion for much longer periods than the half-minute immersion time used; acetic anhydride mixtures were found to be poor solvents for the reaction product, which rapidly separated from solution. The results recorded in Fig. 3 were again obtained from half-minute immersion times, but even within this time the presence of reaction product caused the reaction rate to fall somewhat.

A study of mixtures with 1 : 4-dioxan was of particular significance in view of the unusual stability of the addition compound. This is only possible over narrow concentration ranges, since the 1 : 1 addition compound $C_4H_8O_2,N_2O_4$ crystallises rapidly from mixtures prepared in the 15—85 mol. % dioxan range. Measured rates are given in Table 1. The reaction rates for copper in 0—15 mol. % dioxan solutions lie close to the

TABLE 1. *Rates of reaction (g. of metal per cm.$^2$ per min.) with dioxan–dinitrogen tetroxide mixtures at 15° and 400 r.p.m.*

| Dioxan (mol. %) | Rate | Dioxan (mol. %) | Rate | Dioxan (mol. %) | Rate | Dioxan (mol. %) | Rate |
|---|---|---|---|---|---|---|---|
| | Copper | | | | Zinc | | |
| 3·4 | 0·00038 | 13·5 | 0·00234 | 8·2 | 0·00050 | 89·6 | 0·00015 |
| 5·5 | 0·00047 | — | — | 9·5 | 0·00055 | 94·5 | 0·00008 |
| 9·5 | 0·00085 | 83 | ~0·0 | 12·0 | 0·00081 | — | — |
| 10·6 | 0·00132 | 94·5 | ~0·0 | | | | |

diethyl ether curve (Fig. 1), and in spite of the high stability of the molecular addition compound the reaction rates again indicate the presence of ionic species in solution.

Some cyanides and nitrosamines give extreme examples of type (2) curves, as shown in Figs. 4 and 5. Because of their relatively stronger donor properties, the presence of higher concentrations of ions $(Don)_n,NO^+$ gives a rapid increase in reaction rate on addition of only a few mol. % of the donor. The restrictive effect also sets in at lower solvent concentration, so that under conditions of stirring the reaction rate is falling continuously throughout the 5—100 mol. % solvent-concentration range. Figs. 4 and 5 show that with nitrogen-donor solvents also, stirring may influence the rate of reaction, and may modify slightly the position of the maximum, but does not influence the type of rate curve obtained.

*Reaction Processes.*—We will consider first some general aspects of these processes, and then show how they may be used to explain the shapes of the reaction rate curves. The processes by which a metal atom on a metal surface becomes an ion in solution may be divided into two stages: I, an electronic reaction at the metal surface to give a metal cation; and II, the formation of a solvation or co-ordination sphere round the ion, which is necessary before the cation can be removed from the surface into solution. Process I involves the transfer of electrons from the metal to an electron-acceptor in solution; the ions $H_3O^+$ and $I^+$ perform this function in the reaction of metals with aqueous acid or iodine solutions, and in the present systems simple ($NO^+$) or complex $(Don)_n,NO^+$ ions. It is convenient to regard the metal as consisting not of discrete atoms, but as possessing a fund of electrons; each electron removed leaves a metal cation which is adsorbed at the surface by electrostatic attraction. The cation may be desorbed from the surface (process II) if the liquid medium contains molecules or ions which can solvate the cation, thus decreasing this attraction. This process is therefore somewhat analogous to the dissolution of salts in polar solvents.

Cation desorption may therefore be brought about by polar molecules capable of simple solvation only, or more efficiently by molecules or ions able to donate electrons to the metal ion to give a co-ordination complex. Nitrobenzene and nitromethane are typical polar solvating molecules, and have similar dipole moments and dielectric constants. However, nitromethane is the better solvent for ionic compounds and increases the rate of metal–$N_2O_4$ reactions to a greater extent, indicating that dipole moment in relation to molecular volume is a more satisfactory measure of solvating power than is the dipole

moment alone. Since dinitrogen tetroxide has zero dipole moment it is considered to be a weakly solvating species. The only species common to these media which is capable of co-ordination to the metal ions is the nitrate ion. Previous papers [7-9] have given evidence for the existence of nitrato-anions of zinc and uranium in the solid state and in solution in

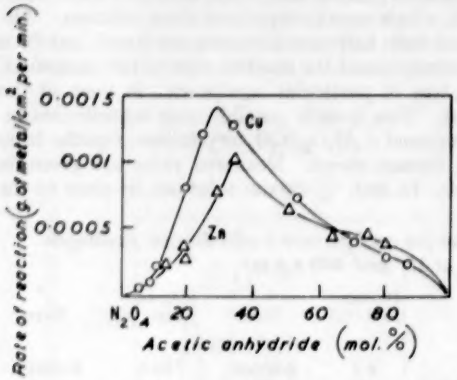
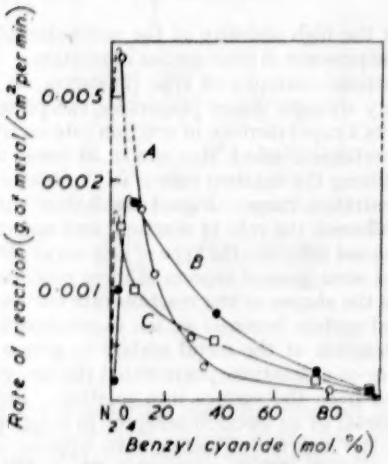


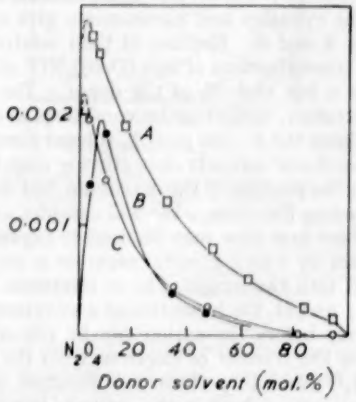

FIG. 3. *Rates of reaction with $N_2O_4$–acetic anhydride mixtures at 15° and 400 r.p.m.*

FIG. 4. *Rates of reaction in $N_2O_4$–benzyl cyanide mixtures.*




*A*, Copper, stirring rate 400 r.p.m.
*B*, Zinc, unstirred.
*C*, Zinc, stirring rate 400 r.p.m.

FIG. 5. *Rates of reaction of copper at 15° with various mixtures.*




*A*, Diethylnitrosamine mixtures, stirring rate 400 r.p.m.
*B*, Phenyl cyanide mixtures, unstirred.
*C*, Phenyl cyanide mixtures, stirring rate 400 r.p.m.

non-aqueous solvents. Desorption of metal ions by nitrate ions would appear to be a favourable process, since co-ordination neutralises the charge on the cation. The concentration of nitrate ions in the bulk liquid phase is unlikely to be sufficient for desorption of metal ions, but it is feasible that the $N_2O_4$ molecule can ionise in the neighbourhood of the unco-ordinated metal cation as a result of the electrostatic forces at the surface.

Preferential adsorption of one component from the liquid mixture on the metal

[7] Addison and Hodge, *J.*, 1954, 1138.
[8] Addison, Hodge, and Thompson, *J.*, 1954, 1143.
[9] Addison and Hodge, *Nature*, 1953, **171**, 569.

surface is also an important factor in these processes. Polar solvent molecules will be adsorbed to a greater extent than the non-polar dinitrogen tetroxide. Of the solvents investigated, nitromethane and methyl cyanide have high dipole moments and the smallest molecular volumes. They are therefore excellent solvating agents, and the results reported here may be interpreted satisfactorily on the assumptions that (*a*) desorption involving solvation by these two solvents occurs more readily than by nitrate-ion co-ordination, and (*b*), except for these two solvents, co-ordination by nitrate ions is the fastest means of removing the metal ions from the metal surface.

*Interpretation of Reaction Rate Curves.*—We may now attempt an analysis of the curves in the light of the principles outlined above.

*Type* (1). It being assumed that nitromethane, by virtue of its high solvating powers, can remove unipositive metal ions from the metal at least as quickly as they are produced, type (1) represents the simplest system, and the shape of the copper–nitromethane curve (Fig. 2) reflects the concentration of $NO^+$ ions throughout the concentration range. It is also consistent that stirring of the metal specimen in the solution should influence only the rate at which $NO^+$ ions reach the surface, and thus the actual reaction rate, without influencing the shape of the curve. Even though zinc is more electropositive than copper, its reaction rate is slower. Zinc ions can leave the metal only in the $Zn^{2+}$ state, and this implies a greater electrostatic attraction between the ion and the metal surface. Since a non-donor molecule such as nitromethane forms a loose solvation cage round the ion, but without direct bonding to it, removal of ions from the surface will be less efficient.

*Type* (2) (Fig. 1). Consider first section *D*(*a*) of curve *D*, where reaction rate is increasing rapidly with concentration of solvent. The solvents which show type (2) curves are poor desorbing agents for the particular metal cation concerned. The concentration of $(Don)_n.NO^+$ ions will increase with the donor properties of the solvent with respect to $NO^+$ ions. Reaction rates of copper increase accordingly in the order nitromethane < diethyl ether < ethyl acetate < phenyl cyanide, benzyl cyanide, methyl cyanide, diethyl nitrosamine.

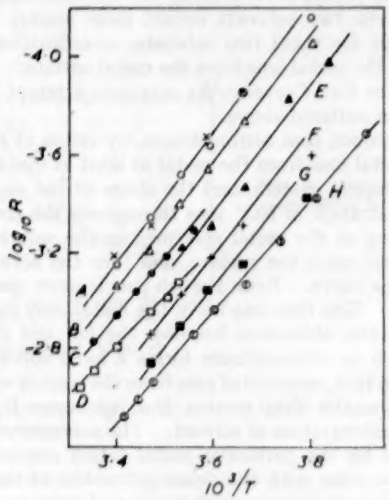
Increase in the concentration of the complex ions will result in a corresponding increase in the reaction rate as long as the metal cations formed can be transferred to the liquid phase with corresponding rapidity. In the presence of these relatively poor solvating liquids desorption of metal ions is carried out by $NO_3^-$ ions. Over section (*a*) of the curve, the dinitrogen tetroxide (and its ionisation products) is assumed to have direct access to the metal surface. The sharp maxima in the curves of this type occur at solvent concentrations much lower than those which represent maximum concentration of reactive ions in the bulk of the liquid. The more polar the solvent, the lower is the solvent concentration at which the maximum occurs; the order of these concentrations is thus broadly the reverse of the list given above. This leads us to suggest that these solvents are preferentially adsorbed at the metal surface, and that the maximum in the rate curve corresponds with the concentration at which the surface is covered by a film of the solvent which is sufficient to restrict severely direct access of the tetroxide. Thereafter [*e.g.*, along section *D*(*b*) of curve *D*, Fig. 1] the concentration of $N_2O_4$, and therefore of $NO_3^-$ ions for desorption of metal ions will decrease, with a corresponding decrease in reaction rates.

Uranium in nitromethane mixtures gives a type (2) curve (Fig. 2). From its general chemistry it seems likely that uranium reaches the $U^{3+}$ stage before desorption. That nitromethane, which desorbs $Cu^+$ readily, is unable to desorb $U^{3+}$ is indicated by the very low reaction rate. The maximum in reaction rate which occurs at a low nitromethane concentration is then the result of preferential adsorption of nitromethane at the metal surface which limits access of the only species ($NO_3^-$) capable of desorbing the more highly charged ion. If reaction took place by the route $U \longrightarrow U^+ \longrightarrow UO^+$, no difficulties in desorption by nitromethane should arise, and a rate curve of type (1) would have been expected.

That the reaction rate is determined by desorption is indicated by two factors. First, it enables the rate curve of type (3) (Fig. 7) obtained with methyl cyanide to be correlated with the curves of type (2) (see below). Secondly, it is supported by the value of the activation energy *E* for the process operating over section (*b*) of the curve. Rates of

reaction $R$ for several mixtures [at concentrations corresponding to section (*b*)] have been determined over a temperature range. The plots of log $R$ against $1/T$ are shown in Fig. 6; the values of $E$ obtained show little variation (mean, $E = 11$ kcal./mole). This clearly

FIG. 6. *Effect of temperature on reaction rates.*




| Plot | Metal | Mixture: $N_2O_4$ with | Stirring rate (r.p.m.) | $E$ (kcal./mole) |
|---|---|---|---|---|
| *A* | Copper | 56 mol. % of $CH_3{\cdot}CO_2Et$ | × 800 | 12 |
| | | | ○ 400 | 12 |
| *B* | Copper | 56 mol. % ,, | Δ Unstirred | 12 |
| *C* | Copper | 46 mol. % ,, | 400 | 10 |
| *D* | Zinc | 64 mol. % ,, | 400 | 9 |
| *E* | Zinc | 7·1 mol. % of $Et_3N{\cdot}NO$ | Unstirred | 12 |
| *F* | Copper | 10 mol. % of $Ph{\cdot}CN$ | 400 | 12 |
| *G* | Copper | 10 mol. % ,, | Unstirred | 12 |
| *H* * | Uranium | 47·5 mol. % of $CH_3{\cdot}NO_2$ | 350 | 10 |

* The rates $R$ recorded on line *H* are magnified by a factor of 100.

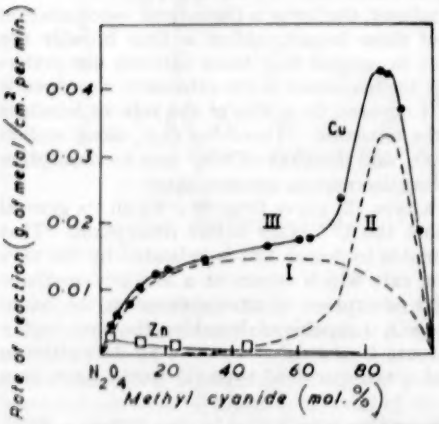
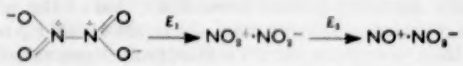


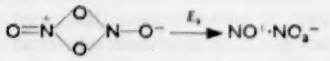

FIG. 7. *Comparison of reaction rates for copper* (III) *and zinc in* $N_2O_4$*–methyl cyanide with that* (II) *of copper in* $N_2O_4$*–nitromethane and with the concentration* (I; *arbitrary units*) *of the ionic complex* $[(Don)_nNO^+]NO_3^-$.

represents the same stage in each reaction, and is associated with one distinct step in the transfer of the free ion on the metal surface to the stage at which it is fully co-ordinated in solution. Since we believe that the $NO_3^-$ ions necessary for desorption are provided

largely by the $N_2O_4$ in the region of the metal surface, the $E$ value of 11 kcal. can be related to the energy of ionisation of $N_2O_4$ under these conditions. The $N_2O_4$ molecule in the reaction step $M^+ + N_2O_4 \longrightarrow M^+NO_3^- + NO^+$ can dissociate via the routes



or



and it is suggested that $E_1 + E_2$, or $E_3$, equals 11 kcal. If $E_3$ is very small,[10] it is significant that $\Delta H$ for the homolytic dissociation of the N–N bond in $N_2O_4$ is 12·9 kcal.[11] Whatever process $E$ may represent, its value indicates that reaction rates are not determined by a diffusion-controlled electron-transfer reaction; for magnesium–aqueous acid [12] and zinc–dinitrogen tetroxide [4] reactions, $E$ is near 5 kcal.

*Type* (3): *Reaction of copper with methyl cyanide mixtures.* The reaction rate curve is shown in Fig. 7. Methyl cyanide combines all the features desirable for high reaction rate. Because of its polar nature and small molecular volume it has good ion-solvating powers comparable with those of nitromethane. Also, it can co-ordinate to a copper ion; the copper salts separated as solid reaction products contain combined methyl cyanide. The results suggest that methyl cyanide is at least as good as the nitrate ion as desorbing agent for unipositive metal ions. Finally, methyl cyanide forms addition compounds with dinitrogen tetroxide, thus enhancing the $(Don)_n.NO^+$ ion concentration. Reaction of copper with methyl cyanide mixtures proceeds vigorously, at rates which are much higher than with any other solvent studied, and are in marked contrast to the rates with benzyl and phenyl cyanide mixtures (Figs. 4 and 5). Because of the desorbing properties of methyl cyanide, there is no longer any reason for the arrest in the rate curve which occurs in type (2) systems, and throughout the concentration range the rate curve should reflect the ionic concentration in solution. This will be determined by two effects. First, the concentration of the ionic complex $[(Don)_n.NO^+]NO_3^-$ passes through a maximum when the liquids are in 1 : 1 mol. ratio; this is represented by the broken curve I in Fig. 7. Secondly, the dielectric constant, and thus the degree of ion separation in the ionic complex, is not at a maximum at the 1 : 1 ratio. In the absence of compound formation the rate curve would follow the broken curve II (as with the nitromethane–copper curve in Fig. 2). Since methyl cyanide is a donor solvent, an ionising medium, and an efficient desorbing agent, the actual variation in reaction rate should represent a summation of these factors. That such is the case is shown by the experimental curve III of Fig. 7. The dielectric constants of methyl cyanide and nitromethane are almost identical; the rate curve rises to a high maximum at the same concentration (85 mol. % solvent) in each system, but the donor properties of methyl cyanide result in a higher concentration of free ions, and a reaction rate which is six times the nitromethane value.

Fig. 7 also emphasises the marked difference between rates of reaction of zinc and copper. Methyl cyanide is apparently unable to desorb $Zn^{2+}$ ions, so that the curve reverts to type (2), resembling that for benzyl cyanide (Fig. 4).

*Influence of Stirring Rates.*—The variation in reaction rate with the speed at which the metal specimen is rotated in the liquid mixture is shown in Figs. 8 and 9. In order to collect the results, an arbitrary vertical axis is employed. The actual reaction rates at any given stirring rate can be obtained by cross-reference between Figs. 8 and 9 and the other Figures where reaction rates are quoted for a constant stirring speed. The reaction rates are influenced by stirring in two ways, and the results are readily interpreted in terms of the principles outlined above.

(*a*) Under conditions in which nitromethane or methyl cyanide can act as desorbing agents, reaction rate increases constantly with stirring rate (Fig. 8). There is then no

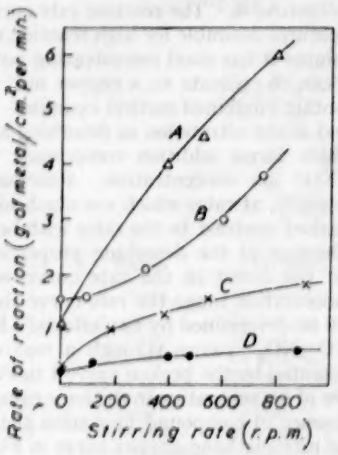
[10] Addison and Lewis, *J.*, 1953, 1869.
[11] Giauque and Kemp., *J. Chem. Phys.*, 1938, **6**, 40.
[12] James, *J. Amer. Chem. Soc.*, 1943, **65**, 39.

restriction on the availability of desorbing species, so that the reactions are diffusion-controlled throughout. For the unstirred reaction of copper with a 92·5 mol. % nitromethane solution, $E$ is near 5 kcal. over the temperature range 0—20°.

(*b*) In solvents with solvating powers lower than that of the nitrate ion (Fig. 9), the reaction rates become constant at stirring rates above about 300 r.p.m. Diffusion from the surface is then faster than desorption, which is thus truly represented by the measurements at 400 r.p.m. in Figs. 1—7. The rate-determining process is again independent of stirring, since the same activation energy is found in stirred and unstirred reactions (Fig. 6).

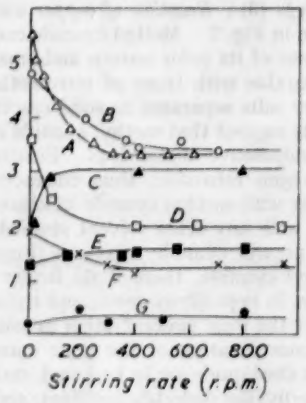
*Other Solvents.*—It was not possible to obtain reproducible results for the reaction of copper with acetic acid–dinitrogen tetroxide mixtures; copper reacts with pure acetic acid at negligible rate, yet reaction rates with the liquid mixtures were of similar magnitude to those for the ether and the ethyl acetate mixtures. Acetic acid differs from the other

FIG. 8. *Systems showing a continuous variation in reaction rate with stirring rate* (15°).



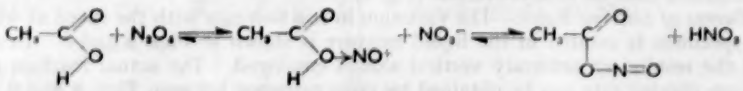

| Metal | Mixture: $N_2O_4$ with |
|---|---|
| *A*, Copper | 91 mol. % of $CH_3{\cdot}NO_2$ |
| *C*, Copper | 72 mol. % ,, |
| *B*, Copper | 3·6 mol. % of $CH_3{\cdot}CN$ |
| *D*, Zinc | 77 mol. % ,, |

FIG. 9. *Systems in which reaction rate becomes independent of stirring rate* (15°).




| Metal | Mixture: $N_2O_4$ with |
|---|---|
| *A*, Uranium | 62·6 mol. % of $CH_3{\cdot}NO_2$ |
| *B*, Copper | 60 mol. % of $CH_3{\cdot}CO_2Et$ |
| *F*, Zinc | 33 mol. % ,, |
| *C*, Zinc | 3·2 mol. % of $Ph{\cdot}CH_2{\cdot}CN$ |
| *D*, Zinc | 9·7 mol. % ,, |
| *E*, Copper | 33 mol. % of $Et_2N{\cdot}NO$ |
| *G*, Zinc | 8·2 mol. % of dioxan |

solvents used in this work in having a hydrogen atom which can be replaced by the NO group. (This reaction is already well illustrated in the conversion of alcohols into alkyl nitrites,[13] and alkyl- or aryl-substituted anilines into the corresponding nitrosamines,[14] by dinitrogen tetroxide.) Such replacement gives rise to the equilibrium:




to which must be added the possible side reaction

$$Cu(NO_3)_2 + 2CH_3{\cdot}CO_2H \rightleftharpoons Cu(CH_3{\cdot}CO_2)_2 + 2HNO_3$$

In each case nitric acid is produced, which may account for the lack of consistency in reaction rates.

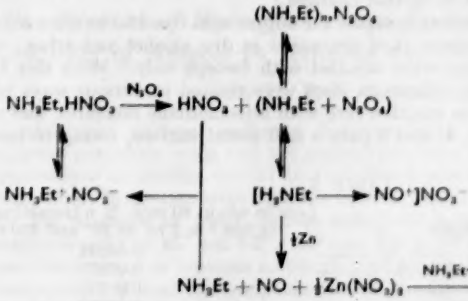
[13] Gray and Yoffe, *J.*, 1951, 1412; *Chem. Rev.*, 1955, **55**, 1069.
[14] Riebsomer, *Chem. Rev.*, 1945, **36**, 157.

Although metal–$N_2O_4$ reaction rates are increased by 'onium donor solvents, π-donor solvents have no such effect. Benzene and nitrobenzene are π-donors, forming solid 1 : 1 compounds with dinitrogen tetroxide.[1] Immersion of copper in tetroxide–benzene mixtures for 20 minutes gave a scarcely detectable weight change. Ionisation of dinitrogen tetroxide in nitrobenzene is enhanced by high dielectric constant, and might have been expected to lead to higher reaction rates with these mixtures. Zinc reacts with the pure tetroxide at the rate of $7{\cdot}5 \times 10^{-4}$ g./cm.$^2$ in 15 minutes at 15° and 250 r.p.m. Over a wide composition range, reaction rates with nitrobenzene–tetroxide mixtures did not exceed $1 \times 10^{-4}$. This is attributed to the feeble solvating and desorbing powers of nitrobenzene, which are presumed to be less than those of the nitrate ion. Results with π-donors are therefore in accord with views already expressed.

*Reactions of Metals with Solutions of Alkylammonium Nitrates in Dinitrogen Tetroxide.*—The rate of reaction of metals with dinitrogen tetroxide is increased on addition of alkylammonium nitrates. Conditions and products of reaction with zinc have been described elsewhere.[7,8] Such solutions have been regarded as "basic" in this solvent system, since the added solute introduces the anion ($NO_3^-$) characteristic of the medium, and reactions such as

$$Zn + 2N_2O_4 + 2NH_2Et{\cdot}NO_3 = (NH_3Et)_2[Zn(NO_3)_4] + 2NO$$

have been regarded as illustrating amphoteric behaviour in this system, being formally analogous to that between zinc and aqueous alkali. However, the simple introduction of $R_4N^+$ and $NO_3^-$ ions into the solution should not in itself enhance reaction rates; no satisfactory reaction mechanism can be postulated on the basis of these ions alone, and the rates are much higher than would result from alteration in dielectric constant of the solution. The studies with solvent mixtures described above suggest that a similar mechanism accounts suitably for these reactions also; this is outlined for the zinc–ethylammonium nitrate solution reaction [7] in the following scheme:




The reactive species in alkylammonium nitrate solutions is therefore again considered to be the $(Don)_n.NO^+$ ion. The amines are strong donors to dinitrogen tetroxides;[15,16] they react explosively with the tetroxide when the pure liquids are mixed at room temperature, but addition compounds can be isolated at low temperatures. The presence of nitric acid stabilises the addition compound in some way, since dilute solutions of the alkylammonium nitrates are relatively stable. This may occur by ternary addition compound formation since compounds of empirical formula $N_2O_4,Et_3N,HNO_3$ and $N_2O_4,2Et_3N,2HNO_3$ have also been isolated.[17] Reaction rates with alkylammonium nitrate solutions are of the same order as with many donor-solvent mixtures. For example, in a 7·1 mol. % diethylammonium nitrate solution, unstirred, zinc reacts at the rate of 0·0016 g./cm.$^2$ per min. at 15°. The reaction rate with a benzyl cyanide solution of the same concentration is 0·0018 unit (Fig. 5).

[15] Comyns, *Nature*, 1953, **172**, 491; *J.*, 1955, 1557.
[16] Davenport, Burkhardt, and Sisler, *J. Amer. Chem. Soc.*, 1953, **75**, 4175.
[17] Addison and Hodge, *Chem. and Ind.*, 1953, 1315.

## Experimental

*Apparatus.*—Copper and zinc were used in the form of rectangular blocks approx. 2·5 cm. long, and 0·5 cm. wide, with a hole of 0·2 cm. diameter drilled near one end. They were machined with precision so that the surface area could be determined accurately by micrometer. The blocks were suspended on a glass hook mounted in an aluminium stirring gland with B.24 cone. The gland was geared to a variable-speed electric motor. About 30 c.c. of the liquid mixture (made up by direct weighing, with precautions against contact with atmosphere) were transferred to a B.24 tube, which was coupled to the stirring gland at the start of the run and was immersed in a thermostat. At the end of the run the block was rapidly withdrawn and washed successively with dry carbon tetrachloride, alcohol, and ether, and its loss in weight determined. Uranium was used in the form of thin discs of approx. 1·4 cm. diameter, 3·5 cm.$^2$ surface area, and 3·0 g. weight. The disc was suspended by a hole (1 mm. diameter) bored near its edge. The experiments were carried out as for copper and zinc, except that because of the longer immersion times it was desirable to fit the tube containing the liquid mixture with two side-arms—one, which served as a vent, carried a phosphoric oxide guard tube, and the other a thermometer whose bulb was immersed in the reaction liquid.

*Purity of Materials.*—Dinitrogen tetroxide was prepared and purified as already described,[18] and organic solvents were carefully purified by accepted methods. Spectroscopically pure copper (Johnson Matthey Ltd.) was used, and the zinc blocks were cast from "AnalaR" granulated zinc. Uranium of very high purity was kindly supplied by the Atomic Energy Research Establishment, Harwell.

*Behaviour of Metals with Liquid Dinitrogen Tetroxide alone.*—Reaction with zinc has already been described.[4] Copper showed only the slightest indication of attack during immersion for many days. A freshly filed disc of uranium retained its bright surface without tarnish, and no loss in weight could be detected after 7 days' immersion. Similarly, no reaction took place when uranium was left in contact with dinitrogen tetroxide diluted with carbon tetrachloride or chloroform for 3 weeks at 25°. (The reactivity of uranium with dinitrogen tetroxide vapour is low at temperatures up to 120°; the metal surface became covered by a very thin film of oxide, and prolonged exposure gave no further changes.)

*Treatment of Metal Surfaces.*—Before reaction the copper and zinc blocks were abraded with a clean file to produce a fresh surface, then degreased in dry alcohol and ether; thereafter during weighing and mounting they were handled with forceps only. With this treatment, reproducible results were obtained. Uranium discs were treated in various ways to examine the influence of surface condition on reaction rate with nitromethane mixtures, and results are shown in Table 2. Treatments 1, 4, and 5 gave a dull metal surface, owing to formation of

Table 2.

| Treatment of uranium discs | Loss in wt. in 60 mol. % nitromethane mixture (g./cm.$^2$ in 2 hr. at 20° and 350 r.p.m.) |
|---|---|
| 1. Acid washed with 2*N*-HCl | 0·00281 |
| 2. Abraded with carborundum powder | 0·00271 |
| 3. Filed | 0·00271 |
| 4. Exposed to atmosphere for 7 days | 0·00298 |
| 5. Heated at 200° for 1 hour | 0·00371 |

uranium salt or oxide at the surface, and gave high values. The freshly filed surface again gave reproducible results.

*Selection of Immersion Periods.*—Long immersion of the metal in the liquid mixture can result in a change in reaction rate due to passivity effects or to the accumulation of soluble reaction products in the solution or of insoluble products at the metal surface. Preliminary measurements were therefore made to determine suitable immersion periods over which reaction rate was constant. Typical experiments for copper and zinc are shown in Table 3.

Over periods up to 4 min. the weight loss was proportional to immersion time for all solvents used (except acetic anhydride). In these measurements surface area suffered negligible change, and weight losses are given in g. rather than g./cm.$^2$. Immersion for 0·5 min. gave weight losses of suitable magnitude, and all results reported for copper and zinc in this paper are based on this immersion time. Uranium reaction rates are slower.

Reaction products are soluble in mixtures containing a large proportion of nitromethane,

[18] Addison, Allen, Bolton, and Lewis, *J.*, 1951, 1289.

TABLE 3. *Influence of immersion time on copper and zinc reaction rates.*

| Metal | Solvent | Solvent (mol. %) | Wt. loss ($10^{-3}$ g.) from metal block for the following immersion times (min. at 15° and 400 r.p.m.) 0·25 | 0·5 | 1·0 | 2·0 | 2·5 | 4·0 |
|---|---|---|---|---|---|---|---|---|
| Cu | $Me{\cdot}NO_2$ | 94 | 6 | 12 | 23 | — | — | — |
| Cu * | Me·CN | 12 | 14 | 28 | 56 | — | — | — |
| Cu | $CH_2{\cdot}CO_2Et$ | 34 | — | 8 | 16 | 33 | — | — |
| Cu | $Et_2N{\cdot}NO$ | 32 | — | 3 | — | 11 | — | 22 |
| Zn | ,, | 3·9 | — | 4·5 | — | 18 | — | 39 |
| Zn | $Ph{\cdot}CH_2{\cdot}CN$ | 39 | — | 2·1 | 4·2 | — | 10·5 | — |
| Zn | ,, | 76 | — | — | 1·9 | 3·7 | — | — |

* At 640 r.p.m.

TABLE 4. *Influence of immersion time on uranium reaction rate in* $N_2O_4$–$CH_3{\cdot}NO_2$ *mixtures.*

| Expt. | Nitromethane (mol. %) | Wt. loss ($10^{-3}$ g./cm.²) from uranium block for the following immersion times (hr. at 20° and 350 r.p.m.) 2 | 4 | 6 | 8 | 10 | 11 |
|---|---|---|---|---|---|---|---|
| 1 | 62·6 | 2·45 | 4·9 | 7·3 | 9·7 | 12·1 | 13·5 |
| 2 | 18·4 | 1·75 | 3·4 | 5·1 | 6·8 | 7·9 | 8·2 |

and weight loss is proportional to immersion time for at least 11 hr. (Expt. 1, Table 4). As the solubility of the reaction product diminishes (Expt. 2) it accumulates ultimately on the metal surface, so that reaction rates decrease after about 7 hr. The reaction rates for uranium given in Figs. 2, 6, and 9 are based on 2-hour immersion periods.

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THE UNIVERSITY, NOTTINGHAM. [*Received, May 10th,* 1956.]

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## 759. *The Kinetics of Hydrogen Isotope Exchange Reactions. Part VI.* The Reactivity of Anisole in Aqueous and Non-aqueous Acidic Media.*

By D. P. N. SATCHELL.

Hydrogen isotope exchange between both aqueous sulphuric and aqueous perchloric acids and the nuclear positions in anisole shows a kinetic dependence on acidity similar to that found previously for other aromatic compounds in contact with aqueous mineral acids. The partial rate factors for the reactions of [*o*-$^3H_1$]anisole and [*p*-$^3H_1$]anisole with 8·53M-aqueous sulphuric acid at 25° are $2{\cdot}3 \times 10^4$ and $5{\cdot}5 \times 10^4$ respectively. The *ortho/para* rate ratio † in aqueous sulphuric acid media, *viz.*, 0·42, is shown to be independent of medium composition over a wide range. [*m*-$^3H_1$]Anisole is deactivated towards hydrogen isotope exchange compared with [$^3H_1$]benzene in both aqueous sulphuric and aqueous perchloric acid. This behaviour is discussed. The partial rate factor for the *meta*-position in 10·43M-aqueous perchloric acid is 0·25. Measurements of the rate of hydrogen isotope exchange between [$^3H_1$]benzene and aqueous perchloric acid media are reported.

In acetic acid–sulphuric acid media the exchange reaction shows a similar kinetic behaviour to that characteristic in aqueous media, and it is concluded that the mechanisms are similar. At the same value of $H_0$, [*o*-$^3H_1$]anisole and [*p*-$^3H_1$]anisole react somewhat less rapidly in acetic acid–sulphuric acid than in sulphuric acid–water : the *ortho/para* rate ratio is 0·55 in the former as compared with 0·42 in the latter medium.

IN Part V* the behaviour of toluene in hydrogen isotope exchange with aqueous mineral acid was described and shown to be in accord with a mechanism for aromatic hydrogen

* Part V, *J.*, 1956, 2743.

† This term implies simply the ratio of the partial rate factors for the *ortho*- and the *para*-position.

isotope exchange previously proposed.[1] The importance of time-variable electrical effects in the exchange process was revealed. We now report work with anisole. A start has also been made in the study of exchange kinetics in non-aqueous acidic media, about which little is known. Acetic acid–sulphuric acid mixtures were the non-aqueous acidic media chosen.

There appears to have been only one previous study of the behaviour of anisole towards hydrogen isotope exchange with aqueous mineral acids. Ingold, Raisin, and Wilson [2] included it in their survey of the behaviour of various aromatic compounds with different aqueous acids, when they established the electrophilic nature of the exchange process in such systems. They found that, at room temperature, in contact with deuterosulphuric acid of greater concentration than the monohydrate, three nuclear positions of anisole exchange rapidly and the remaining two (the *meta*-positions) much more slowly. They studied benzene under similar, heterogeneous conditions and also recorded approximate sulphonation losses for both compounds. Their experiments were only semiquantitative but the tentative deduction may be made that, in 54·5 mole % aqueous sulphuric acid, the exchange at a *meta*-position in anisole is less rapid than at a position in benzene and also less rapid than the total rate of sulphonation of anisole.

In the present investigation the rate of reaction of the three nuclear, monodeuterated anisoles with sulphuric acid–water mixtures has been studied at 25°. Each compound was allowed to react with a series of media in order to discover the dependence of its exchange rate upon acidity. The *meta*-isomer was also studied with a series of perchloric acid–water mixtures.

Two previous investigations of the behaviour of anisole towards hydrogen isotope exchange with acetic acid–sulphuric acid media have been recorded. (1) Brown, Wilzbach, and Urry [3] dissolved anisole in deuteroacetic acid containing a trace of sulphuric acid, and their semiquantitative experiments, conducted at 90°, revealed exchange at three positions only, demonstrating the expected strong *ortho–para*-direction and electrophilic nature of the exchange process. (2) Lauer and Day [4] measured the rate of loss of deuterium from the *ortho*- and *para*-positions to a light sulphuric acid–acetic acid medium. Their reaction mixtures had the approximate molar composition anisole : sulphuric acid : acetic acid, 0·01 : 0·001 : 0·05. The *ortho*/*para* rate ratios at 100° and 80° were found to be 0·52 and 0·33 respectively. Discussion of these results is deferred.

In the present study the *ortho*- and *para*-deutero-isomers were each allowed to react with a series of acid mixtures at 25°. The reaction mixtures were homogeneous, the acid solvent being initially completely light and present in large excess. The same was true of the aqueous reaction mixtures.

## Experimental

*Preparation of Deutero-compounds.*—(a) *Monodeuteroanisoles.* The standard Grignard procedure was used. The ethereal solutions of the Grignard reagents prepared from *o*- and *p*-bromoanisole and from *m*-iodoanisole were decomposed with 99·7% deuterium oxide. The solid products were decomposed in each case with ammonium chloride, and the ether layers separated and dried. Fractional distillation led to anisole in yields of about 70%, the products containing probably about 90 mole % of heavy isomer. All three deutero-isomers have been previously prepared, and the essentials of their infrared spectra recorded.[5] The samples prepared in the present work had spectra similar to those recorded, except that the peaks occurring at 8·90 $\mu$ for the *ortho*- and at 12·65 $\mu$ for the *meta*-isomer were doublets.

(b) [$^2H_1$]*Benzene.* This was prepared as previously described.[6]

*Other Materials.*—(*a*) The ordinary anisole used was a redistilled specimen, of b. p. 154°.

(*b*) The acetic acid–sulphuric acid mixtures were made up by weight from 100% sulphuric acid and anhydrous acetic acid, the former prepared by addition of oleum to the 95% acid until

[1] Gold and Satchell, *J.*, 1955, 3609.
[2] Ingold, Raisin, and Wilson, *J.*, 1936, 1637.
[3] Brown, Wilzbach, and Urry, *Canad. J. Res.*, 1949, **27**, *B*, 398.
[4] Lauer and Day, *J. Amer. Chem. Soc.*, 1955, **77**, 1904.
[5] Hall, Piccolini, and Roberts, *ibid.*, p. 4540.
[6] Bryce-Smith, Gold, and Satchell, *J.*, 1954, 2743.

the f. p. reached 10·4°. The anhydrous acetic acid was prepared by azeotropic distillation of "AnalaR" acetic acid with benzene. It had m. p. >16·6°. (*c*) The concentrations of the aqueous acid mixtures were determined by titration.

*Procedure for Exchange Experiments.*—The reactions of the deutero-compounds were studied under homogeneous conditions at 25°.

(a) *Sulphuric acid–water media.* [*p*-$^2H_1$]Anisole was allowed to react with five different sulphuric acid–water mixtures having $H_0$ (Hammett's acidity function [7]) values varying from −1·50 to −3·44. For [*o*-$^2H_1$]anisole, also studied with five mixtures, the $H_0$ values varied from −2·25 to −3·59. [*m*-$^2H_1$]Anisole was allowed to react with three mixtures, the $H_0$ values varying from −4·78 to −6·32.

The experimental procedure was similar to that previously used with benzene and toluene.[8] Small measured samples of deutero-compound were dissolved in a large excess of a given acid mixture contained in flasks fitted with ground-glass stoppers and having an additional sealing of Apiezon Q compound. Four or five samples were used with each acid–water mixture. After an appropriate period in a thermostat bath at 25° a flask was opened and a measured amount of light anisole added to its contents which, after resealing of the flask, were agitated for 15 min., thus equilibrating the dissolved and the added anisole. The resulting anisole sample was separated and analysed for the deutero-isomer by infrared spectroscopy.[8] In this way the exchange reaction could be followed.

For the *ortho*- and *para*-isomers ~0·15 ml. samples were dissolved each in 400-ml. of acid and equilibrations were carried out with ~1·1 ml. of light anisole. Since the solubility of anisole in sulphuric acid–water increases markedly when $-H_0$ becomes greater than ~4·5, the *meta*-isomer can be used with smaller acid samples. Usually ~0·15 ml. of deutero-compound was dissolved in 100 ml. of acid, and equilibration performed with ~0·5 ml. of light anisole.

For the fastest rates studied a small correction was made for the time occupied by shaking when this interval was no longer negligible compared with the reaction time.

By reversing the procedure described it is also possible to measure the rate of destruction of anisole by the media used. It is important that this rate should be small compared with the rate of exchange, since otherwise measurement of the latter becomes either inaccurate or impossible.

To measure the rate of destruction of anisole, samples of light compound were dissolved and finally that remaining in solution was equilibrated with a suitable light–heavy mixture. (When necessary the acid was diluted to prevent exchange during this equilibration.) As previously mentioned,[8] the reversed procedure is analytically less sensitive than the normal procedure when the solubility is low. However, for anisole in the media with $-H_0$ values >4·5 it can be made of comparable accuracy, giving figures reproducible within ±8%.

The results obtained with the three anisoles are collected in Tables 1, 2, and 5. Their discussion is deferred.

(b) *Sulphuric acid–acetic acid media.* Similar analytical methods can be used with these media by working at somewhat higher concentrations. In practice, ~1 ml. of deuteroanisole was dissolved in 100 ml. of acid mixture. At appropriate intervals 20 ml. samples were removed and run into ~200 ml. of water, thus effectively stopping the exchange reaction and providing a solution which could be equilibrated with light compound as described above.

The rates of destruction of anisole in some of these media were also studied. [*p*-$^2H_1$]Anisole was studied with six acid mixtures, and [*o*-$^2H_1$]anisole with three. The results are collected in Table 3 and 4.

(c) *Perchloric acid–water media.* [*m*-$^2H_1$]Anisole was studied with four, and [$^2H_1$]benzene with three acid mixtures in the $H_0$ range −5·45 to −7·35. Both exchange rates and rates of destruction were studied. The procedure was similar to that described for aqueous sulphuric acid except that 30-ml. samples of acid could be used. The results are given in Tables 6 and 7.

## Discussion

*Behaviour of the* ortho- *and* para-*Isomers.*—(a) *Sulphuric acid–water media.* The rate of destruction of anisole in the mixtures used for these isomers was found to be negligible compared with the exchange rates. The solutions remained clear and colourless. Under the experimental conditions used the exchange reaction is a first-order process.[9] In Fig. 1

[7] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co. Inc., New York, 1940.
[8] Gold and Satchell, (*a*) *J.*, 1955, 3619; (*b*) *J.*, 1956, 2743; (*c*) *ibid.*, p. 1635.
[9] *Idem*, *Quart. Rev.*, 1955, **9**, 51.

the logarithms of the first-order rate constants ($\lambda$) are plotted against $-H_0$. Both the *ortho*- and the *para*-isomer give straight-line plots. The two slopes are the same, within experimental error, and have the value 1·18. Because the range of media studied for the two isomers was roughly the same, parallel straight-line plots were predictable on the basis of the previously suggested mechanism for the reaction. The value of the slope is also acceptable in the light of previous discussion.[10]

Data referring to [$^2H_1$]benzene are also included in Fig. 1. The benzene plot was, of course, obtained from the results of experiments in more concentrated acid mixtures.[8] If it is permissible to extrapolate either, or both, of the benzene and anisole graphs, then the partial rate factors for the *ortho*-and *para*-positions of anisole may be calculated at any desired medium composition.

Although it is certain from the general kinetic behaviour [1,8] that, except in special cases which involve deactivation of the reacting species by the solvent, the graphs of log $\lambda$

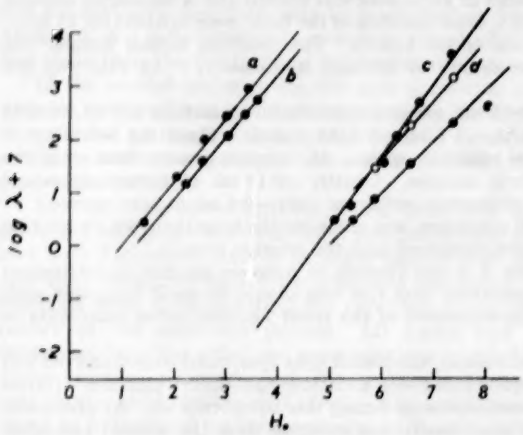



FIG. 1. *Variation of exchange rate with acidity in aqueous sulphuric and perchloric acid.*

*a*, [*p*-$^2H_1$]Anisole; *b*, [*o*-$^2H_1$]anisole; *c*, [$^2H_1$]benzene; *d*, [$^2H_1$]benzene; *e*, [*m*-$^2H_1$]anisole. *a*—*c*, in $H_2SO_4$; *d*, *e*, in $HClO_4$.

against $-H_0$ will have a slope close to unity over a very wide range of composition, so that extrapolation will certainly give fairly accurate comparisons between compounds studied in different acid regions, nevertheless how far such graphs may be extrapolated without *any* error cannot be stated. (It was hoped that the study of the *meta*-isomer would throw

TABLE 1. *Rate of loss of deuterium from* [p-$^2H_1$]*anisole in aqueous sulphuric acid at* 25°.

| $H_2SO_4$ (M) | 3·51 | 4·86 | 5·95 | 6·77 | 7·59 |
|---|---|---|---|---|---|
| $-H_0$ (1) | 1·44 | 2·05 | 2·59 | 3·00 | 3·44 |
| $10^7\lambda$ (sec.$^{-1}$) | 2·93 | 18·5 | 88·0 | 255 | 839 |

TABLE 2. *Rate of loss of deuterium from* [o-$^2H_1$]*anisole in aqueous sulphuric acid at* 25°.

| $H_2SO_4$ (M) | 5·18 | 5·90 | 6·82 | 7·34 | 7·88 |
|---|---|---|---|---|---|
| $-H_0$ (1) | 2·22 | 2·55 | 3·06 | 3·34 | 3·60 |
| $10^7\lambda$ (sec.$^{-1}$) | 14·9 | 36·3 | 121 | 291 | 521 |

some light on this, but unfortunately it did not.) Clearly, the smaller the extrapolation the smaller the uncertainty introduced. In the present case an extension of the anisole plots over one $H_0$ unit towards higher acidities seems unlikely to introduce any great error, and the same is probably true for an extension of the benzene graph over one, or even two, $H_0$ units in the opposite direction. Hence the partial rate factors for the *ortho*- and *para*-positions of anisole in, say, 8·53M-aqueous sulphuric acid ($H_0 = -4·0$) can be

[10] Gold and Satchell, *J.*, 1955, 3622.

calculated with some confidence. However, in the general case of a comparison of the reactivities of compounds studied in widely different acidity regions, *i.e.*, compounds of widely different reactivity, our present ignorance as to how much the slopes of the graphs will alter with changes in medium makes such a comparison somewhat uncertain. Further work should provide information serving to make such comparisons more precise.

The partial rate factors for the *ortho*- and *para*-positions of anisole in 8·53M-aqueous sulphuric acid are found to be $2{\cdot}3 \times 10^4$ and $5{\cdot}5 \times 10^4$ respectively at 25°. The *ortho*/*para* rate ratio has the constant value of 0·42 between 3·5M- and 7·5M-acid. The partial rate factors for bromination by molecular bromine are $0{\cdot}8 \times 10^8$ and $70 \times 10^8$ at the *ortho*- and *para*-positions respectively.[11] The difference from exchange is marked. As for toluene,[8b] the exchange behaviour of anisole is more like that found for its nitration, which [12] involves an *ortho*/*para* rate ratio of the same order as 0·42.

Another comparison of interest is that between the reactivities of [*o*-$^2H_1$]anisole and *p*-methyl[*o*-$^2H_1$]phenol (for which see Part II [1]). In 8·53M-sulphuric acid the rate ratio

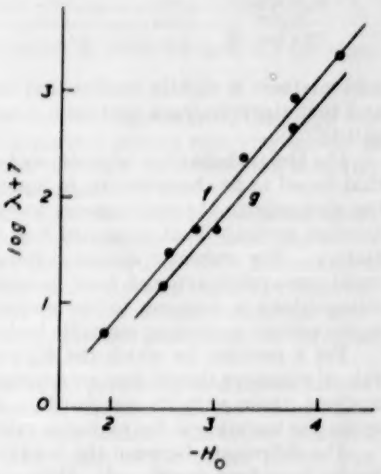



FIG. 2. *Variation of exchange rate with acidity in acetic acid–sulphuric acid.*
*f*, [*p*-$^2H_1$]Anisole; *g*, [*o*-$^2H_1$]anisole.

is 6·5, *p*-cresol reacting the faster. The partial rate factor for the *meta*-position in toluene in this medium will be close [8b] to 1·9. If the hydroxyl and the methyl group be supposed to activate the position *ortho* to the hydroxyl group in *p*-cresol independently and additively, then the hydroxyl group is found to activate an *ortho*-position 3·4 times more than a methoxyl group. Thus the partial rate factor for the *ortho*-position in phenol would, on this basis, be expected to be about $7{\cdot}8 \times 10^4$. (How far, and in what circumstances, partial rate factors found for monosubstituted benzenes can be used in this way to reproduce the reactivities of polysubstituted molecules is not yet known. That the procedure is admissible in some cases seems, however, quite likely.)

(b) *Sulphuric acid–acetic acid media.* In these media the rate of destruction of anisole was found to be not entirely negligible compared with the exchange rate. For instance, in the most acidic mixture used it was about one-twentieth of the exchange rate. In calculating the exchange rate constants (λ) small corrections were made to allow for this loss. The values of these constants for the *ortho*-and the *para*-isomer, given in Tables 3 and 4, are regarded as accurate to ±10%. The fate of the lost anisole is unknown.

The values of $H_0$ quoted in Tables 3 and 4 were taken from Hall and Spengeman's data,[13] it being assumed, for lack of quantitative information to the contrary, that the addition of 1 ml. of anisole to 100 ml. of an acetic acid–sulphuric acid mixture will cause no

[11] de la Mare and Vernon, *J.*, 1951, 1764.
[12] Bunton, Minkoff, and Reed, *J.*, 1947, 1416.
[13] Hall and Spengeman, *J. Amer. Chem. Soc.*, 1940, **62**, 2487.

change in its $H_0$ value. (The actual change is probably quite small.) In Fig. 2, log λ for both isomers is plotted against $-H_0$. The resulting graphs are parallel straight lines with a slope of 1·18. This slope is identical with that found in aqueous sulphuric acid where, as has been seen, parallel straight-line plots are also obtained. The behaviour in the two media is therefore very similar. The only differences are that the exchange rate in acetic

TABLE 3. *Rate of loss of deuterium from* [p-$^2H_1$]*anisole in acetic acid–sulphuric acid media at 25°.*

| $H_2SO_4$ (M) | 0·232 | 0·632 | 0·916 | 1·72 | 2·68 | 3·52 |
|---|---|---|---|---|---|---|
| $-H_0$ [10] | 1·93 | 2·56 | 2·80 | 3·28 | 3·76 | 4·18 |
| $10^7\lambda$ (sec.$^{-1}$) | 5·0 | 30·0 | 50·0 | 230 | 820 | 2100 |

TABLE 4. *Rate of loss of deuterium from* [o-$^2H_1$]*anisole in acetic acid–sulphuric acid media at 25°.*

| $H_2SO_4$ (M) | 0·550 | 1·23 | 2·64 |
|---|---|---|---|
| $-H_0$ [10] | 2·49 | 3·00 | 3·73 |
| $10^7\lambda$ (sec.$^{-1}$) | 14·0 | 51·0 | 450 |

acid mixtures is slightly smaller that that in the aqueous solvent with the same $H_0$ value, and that the *ortho*/*para* rate ratio is somewhat larger in acetic acid, being 0·55 instead of 0·42.

The kinetic behaviour in acetic acid–sulphuric acid media is clearly exactly analogous to that found to be characteristic in aqueous acidic media in general.[1,8] The mechanism of the exchange in the non-aqueous solvent must therefore be similar to that operative in aqueous media. That suggested [1] on the basis of the parallelism with $H_0$ remains satisfactory. The aromatic species is considered to take up a proton from the solvent in a rapid pre-equilibrium and then to undergo a slow intramolecular rearrangement, finally relinquishing a deuteron to the medium. Such a mechanism is clearly possible in any acidic solvent containing ionisable hydrogen.

For a medium for which the $H_0$ values have not been measured, the variation in the rate of exchange should give an approximate indication of how the acidity function for the medium varies with its composition. In a solvent containing both Lewis and Brönsted acids, the variation in the exchange rate should reflect only the potency of the latter.

The differences between the behaviour found in the acetic and aqueous sulphuric acid media have been mentioned. Differences in detailed behaviour in different acidic media have been found before and are discussed elsewhere.[10] At least three distinct effects appear to be involved. First, differences in slope shown by the same compound in different media are thought to arise largely from the change in those solvent properites which affect solubility.[10] Secondly, part at least of any difference in exchange rate shown by the same compound in different media at the same $H_0$ value is probably due to the non-coincidence of the measured $H_0$ scales at present available. When these scales receive their definitive mutual adjustment some of the detailed differences in exchange behaviour found at present will probably be reduced. In the present work a third effect has been met for the first time in connection with hydrogen exchange: it appears that the relative displacement of the rates of reaction of two deutero-isomers of the same aromatic molecule, on change from one medium to another, is not necessarily the same. In the present case this gives rise to a higher *ortho*/*para* rate ratio in acetic acid than in aqueous media. Quite why *ortho*-substitution should be favoured in acetic acid media is not clear.

There is a possible discrepancy between the present results and those of Lauer and Day.[4] These authors found values for the *ortho*/*para* rate ratio in acetic acid–sulphuric acid media which imply a value of 0·1 or less at 25°. This value is in only qualitative agreement with 0·55. How much of the difference can be attributed to the fairly large difference of medium is not known.

*Behaviour of the* meta-*Isomer.*—(a) *Sulphuric acid–water media.* It has unfortunately not been possible to measure the exchange rate of [*m*-$^2H_1$]anisole in aqueous sulphuric acid. When this compound was studied by the methods described there appeared to be exchange,

but when the rate of destruction was measured in the same media it became apparent that the measured exchange could be completely accounted for by this alone, *i.e.*, the rate of loss of anisole in these solutions was the same, within experimental error, whether it was calculated from the results of experiments in which the deutero-isomer was dissolved, assuming no exchange, as when calculated on the basis of experiments in which the light compound was dissolved.

To obtain conveniently measurable reaction rates the media used had $H_0$ values ranging between −4·78 and −6·23. The anisole solutions became pink after a time and some solid was precipitated. The destruction rates were, somewhat surprisingly, roughly of the first order. The approximate (±20%) first-order constants ($k$) are given in Table 5. The

TABLE 5.* *Rate of destruction of anisole in aqueous sulphuric acid at 25°.*

| | | | |
|---|---|---|---|
| $H_2SO_4$ (M) | 10·09 | 11·00 | 12·91 |
| $-H_0$ (?) | 4·78 | 5·27 | 6·23 |
| $10^7 k_H$ (sec.$^{-1}$) | 0·84 | 5·9 | 230 |
| $10^7 k_D$ (sec.$^{-1}$) | 0·81 | 6·0 | 210 |

* $k_H$ and $k_D$ = rate constants calculated from experiments in which the light and the heavy compound, respectively, were dissolved.

rate is seen to increase steeply with acidity. If log $k$ is plotted against $-H_0$ the graph has a slope of about 1·7. It is probable that the most important process removing anisole is sulphonation. That other, though possibly subsequent, processes are involved is, however, evident from the examination of solutions kept for some time.

That the rates of destruction based on experiments with heavy and light isomers agree, if exchange is assumed absent, means in practice that the exchange rate in all the media studied must be at least about five times slower than the destruction rate. Examination of Fig. 1, which contains the benzene exchange data, the values given in Table 5 being borne in mind, shows that where $H_0 = -5{\cdot}0$, and probably in higher acidities also, the *meta*-position in anisole must be appreciably deactivated towards exchange in aqueous sulphuric acid.

(b) *Perchloric acid–water media.* By using concentrated perchloric acid media instead of sulphuric acid, sulphonation could be avoided. Anisole, however, still proved unstable. When it was dissolved a yellow-green colour was immediately formed; the colour darkened with time and solid was eventually precipitated. The origin of the colour (which was different from that which eventually formed in the sulphuric acid media) is unknown. The precipitate was presumably anisole which had undergone oxidation or polymerisation. Once a small amount of precipitate had formed it became difficult to separate the anisole and acid phases after the equilibration process, so that study of the rate of reaction of anisole in these media was restricted to the period during which the solutions remained clear. Experiment showed, somewhat surprisingly, that the rate of destruction of anisole was negligible up to the point when solid began to be precipitated. After this point visual examination indicated that, at any rate in the most concentrated acids used, decomposition was rapid. The destruction is therefore possibly autocatalytic. The period which elapses before appreciable decomposition sets in is shorter the stronger the acid. During this period, for acid mixtures having $H_0$ values between −5·45 and −7·35, it was possible to follow the exchange reaction of [*m*-$^2H_1$]anisole over about a quarter of its life in each case. It is usually desirable in kinetic work to follow reactions further than this, but the first-order rate constants obtained (Table 6) were reproducible to ±10%, and are regarded as reliable.

In order to discover whether the *meta*-isomer was deactivated towards exchange in these media compared with benzene, it was necessary to measure the benzene exchange rates. Benzene is much more stable than anisole in perchloric acid and the exchange reaction can be followed over many half-lives without complication arising from appreciable destruction of benzene. The results for three acidities are given in Table 7. It is clear from the values given in Tables 6 and 7 that the *meta*-position in anisole is deactivated towards exchange in concentrated aqueous perchloric acid.

The $H_0$ values quoted in Tables 6 and 7 were obtained from an extrapolation of Hammett and Deyrup's data [14] which only extend to 10·15M-acid. They are probably accurate to better than ±0·2 unit. The plot thus obtained of log λ against $-H_0$ for benzene in aqueous perchloric acid has a slope of 1·12 compared with 1·36 in aqueous sulphuric acid (Fig. 1). The exchange rate in the two media is the same when $H_0 = -5·80$.

TABLE 6. *Rate of loss of deuterium from* [m-$^2H_1$]*anisole in aqueous perchloric acid at 25°.*

| | | | | |
|---|---|---|---|---|
| $HClO_4$ (M) | 10·04 | 10·43 | 11·01 | 11·71 |
| $-H_0$ [14] | 5·45 | 5·85 | 6·55 | 7·35 |
| $10^7\lambda$ (sec.$^{-1}$) | 3·00 | 7·20 | 32·4 | 200 |

TABLE 7. *Rate of loss of deuterium from* [$^2H_1$]*benzene in aqueous perchloric acid at 25°.*

| | | | |
|---|---|---|---|
| $HClO_4$ (M) | 10·43 | 11·01 | 11·71 |
| $-H_0$ [14] | 5·85 | 6·55 | 7·35 |
| $10^7\lambda$ (sec.$^{-1}$) | 28·2 | 175 | 1350 |

The plot of log λ against $-H_0$ for [*m*-$^2H_1$]anisole has a slope of 0·98 (Fig. 1). The slope shown by the *ortho*- and the *para*-isomer in sulphuric acid is 1·18. Thus for both benzene and anisole the use of perchloric acid results in a lower slope. The partial rate factor for hydrogen isotope exchange at the meta position is found to be 0·25 in 10·43M-aqueous perchloric acid.

The results described confirm and amplify the tentative deductions which may be drawn from the work of Ingold, Raisin, and Wilson.[2] The conclusion is inescapable: in strongly acidic media the *meta*-position in anisole is deactivated towards hydrogen isotope exchange. This conclusion presents no theoretical anomaly: one simply assumes that the inductive effect of the methoxyl group is sufficiently powerful to deactivate the *meta*-position in spite of any secondary relay of its very strong tautomeric activation of the *ortho*- and *para*-positions. The present work being the only instance of a direct measurement of the reactivity of the *meta*-position in anisole, the results present no real experimental anomaly either. However, two indirect estimates of the *meta*-reactivity are available and they both predict a slight activation. These estimates are based on experiments with dimethoxybenzenes and the assumption that substituents affect reactivity independently and additively. de la Mare and Vernon [11] have argued, on this basis, that for bromination by molecular bromine in acetic acid the partial rate factor at the *meta*-position should be 1·7. Similarly for alkylation by $Ph_2CH_2^+$ in dilute sulphuric acid–acetic acid media a value of 2·7 can be predicted.[15] There seem to be three possible explanations of this descrepancy:

(i) The *meta*-position *is* activated towards bromination and alkylation yet deactivated towards exchange. This is possible but seems unlikely.

(ii) In the strongly acidic media necessary to effect *meta*-exchange, anisole becomes deactivated by the solvent in a way similar to that postulated for nitro-compounds in connection with their nitration in such media.[16] For anisole this deactivation would arise from hydrogen bonding or protonation at the methoxyl oxygen. At first sight this explanation is attractive, but deactivation by this means would presumably increase steeply with increasing acidity and cannot easily be reconciled with the observed linear dependence of exchange rate on $H_0$, the gradient of which seems very reasonable when compared with that of the benzene plot, the results in sulphuric acid being borne in mind.

(iii) Partial rate factors obtained for monosubstituted benzenes cannot always be used to predict the reactivities of polysubstituted molecules, and *vice versa*. This appears the most likely explanation of the anomaly mentioned. Further experiments on the exchange rates of the dimethoxybenzenes should throw more light on the point.

KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, May 23rd,* 1956.]

[14] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721.
[15] Personal communication from Dr. V. Gold and Mr. D. Bethell.
[16] Gillespie and Norton, *J.*, 1953, 971.

## 760. *The Dissociation Pressure of Cadmium Oxide.*

By I. G. F. Gilbert and J. A. Kitchener.

The partial pressure of cadmium over solid cadmium oxide has been determined between 880° and 1100° c by an accurate form of the entrainment method. The influence of increased oxygen pressure, and comparison with thermodynamic calculations, establish that the vapour is almost completely dissociated. The standard Gibbs free energy of the dissociation CdO (s) = Cd (g) + ½$O_2$ (g) is found to be

$\Delta G^\circ$ (at 1150—1374° K) ($\pm$150°) = 86,120 ($\pm$2900) − 48·84 ($\pm$2·5)$T$ (cal. mole$^{-1}$)

Brewer and Mastick [1] have recently concluded from examination of earlier, approximate, data for the sublimation pressure of cadmium oxide that the vapour of this substance, like those of mercury(I), zinc,[2] and lead(II) oxides, is probably almost completely dissociated. The partial pressures of cadmium (free or combined) in equilibrium with solid cadmium oxide in presence of nitrogen and in pure oxygen have now been determined by an accurate form of the entrainment method.

### Experimental

*Method.*—The reaction vessel is shown in Fig. 1, and is a development of that used by Kitchener and Ignatowicz,[4] the inlet tube being sealed directly in the hot zone to the tube

Fig. 1.

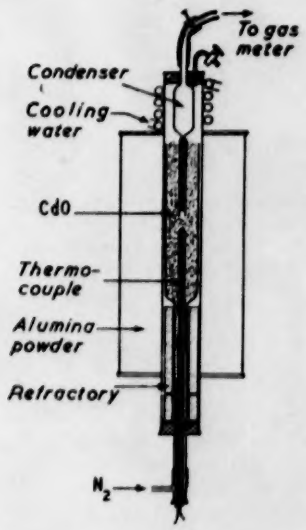
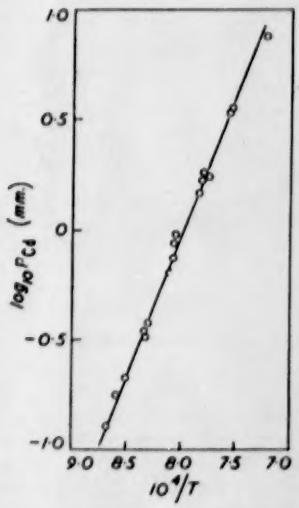



Fig. 2.




containing the cadmium oxide. The oxide (Hopkin and Williams) was previously sintered at *ca.* 1000°. Temperature was measured to $\pm$1° by a platinum/platinum–rhodium thermocouple, and maintained within $\pm$1° by an energy-regulator.

Nitrogen from a cylinder ("oxygen-free"; <0·001% of oxygen) and oxygen, also from a cylinder, used as the entraining gases, were dried with anhydrous magnesium perchlorate.

[1] Brewer and Mastick, *J. Chem. Phys.*, 1951, **19**, 834.
[2] Pourbaix, *Bull. Soc. chim. Belg.*, 1944, **53**, 159.
[3] Richardson and Webb, *Trans. Inst. Min. Met.*, 1955, **64**, 529.
[4] Kitchener and Ignatowicz, *Trans. Faraday Soc.*, 1951, **47**, 1278.

Gas volumes were measured with a Hyde-pattern wet-test meter, calibrated to ±0·2% under closely similar conditions.

The quantity of cadmium carried over into the condenser was determined by slow electrodeposition from weakly alkaline cyanide solution; the method was reliable to ±0·8% for the small quantities collected in these experiments.

*Procedure.*—After the furnace had attained a steady temperature, the condenser was inserted and sealed in place with picein wax. Gas was passed through the bed of oxide (but not through the condenser) to remove air. In the actual determination, only part of the gas stream flowed through the condenser, its volume being measured by the gas-meter. This procedure was to eliminate back-diffusion. At the end of the run, the condenser was quickly removed from the furnace. The deposited cadmium was dissolved in dilute hydrochloric acid, and chloride (which interferes with the analysis) removed by evaporation with dilute nitric acid.

The quantity of cadmium diffusing into the condenser during the preparatory period was found to be negligible.

*Results.*—The partial pressure of cadmium ($p_{Cd}$, in mm. Hg,) was calculated by the ideal-gas laws, with use of the formula

$$p_{Cd} = \frac{(P + p)}{1 + (112{\cdot}4/R)[V(P - p_w)/Tw]}$$

where $P$ (mm.) is the atmospheric pressure, $p$ (mm.) is the (small) excess of pressure in the furnace, $T$(°K) the temperature of the gas meter, $p_w$ (mm.) the parial pressure of water vapour at $T$ °K, $V$ (l.) the volume of permanent gas collected, and $w$ (g.) the weight of cadmium deposited.

| Temp. (c) | Press. of Cd (mm.) | Total gas flow rate (c.c./min.) | Temp. (c) | Press. of Cd (mm.) | Total gas flow rate (c.c./min.) | Temp. (c) | Press. of Cd (mm.) | Total gas flow rate (c.c./min.) |
|---|---|---|---|---|---|---|---|---|
| | | | Carrier gas : nitrogen | | | | | |
| 880° | 0·132 | 88 | 958° | 0·630 | 30 | 1009° | 1·72 | 220 |
| 890 | 0·179 | 120 | 963 | 0·740 | 30 | 1010 | 1·69 | 110 |
| 903 | 0·218 | 66 | 966 | 0·865 | 40 | 1051 | 3·33 | 150 |
| 927 | 0·345 | 125 | 968 | 0·939 | 50 | 1053 | 3·51 | 78 |
| 928 | 0·328 | 88 | 1001 | 1·42 | 76 | 1053 | 3·51 | 200 |
| 934 | 0·375 | 50 | 1006 | 1·65 | 140 | 1101 | 7·36 | 100 |
| | | | Carrier gas : oxygen | | | | | |
| 925 | 0·005 | — | 983 | 0·015 | — | | | |

*Results.*—These are shown in the Table. There is seen to be no systematic variation of $p_{Cd}$ with flow-rate, indicating that a true equilibrium had been reached and measured.

Fig. 2 shows that, with an inert entraining gas, log $p_{Cd}$ is linear with $1/T$ over the range 880—1100° c within experimental error. The least-squares line is given by :

$$\log_{10} p_{Cd}\ (\text{mm.}) = 10{\cdot}008 - 12{,}548/T \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The standard deviation of the points from the line is ±0·029.

## Discussion

The results obtained with oxygen as the entraining gas are smaller by a factor of about 80 than those with nitrogen, demonstrating that oxygen takes part in the equilibrium studied, and that the proportion of molecular cadmium oxide in the vapour above the oxide in nitrogen is certainly very small. In fact, the observed quantities of cadmium obtained with oxygen accord, within the experimental error, with the assumption of complete dissociation.

On this basis, the equilibrium constant ($K = p_{Cd} \cdot p_{O_2}^{\frac{1}{2}}$) for the decomposition

$$CdO\ (s) = Cd\ (g) + \tfrac{1}{2}O_2\ (g)$$

follows from equation (1), as

$$\log_{10} K\ (\text{atm.}^{3/2}) = 10{\cdot}691 - 18{\cdot}822/T \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and hence the standard Gibbs free energy of the reaction, $\Delta G^\circ$, is given by :

$$\Delta G^\circ\ (\text{at } 1150\text{—}1374°\text{ K})\ (\pm 150°) = 86{,}120\ (\pm 2900) - 48{\cdot}84\ (\pm 2{\cdot}5)\ T\ (\text{cal. mole}^{-1})$$

To confirm the conclusion that vaporization occurs only through dissociation, these results have been compared with thermodynamic calculations based on a calorimetric value of the heat of formation of CdO (s),[5] vapour-pressure data for cadmium metal, and heat content and entropy data (see Appendix). The resulting equation for log $p_{Cd}$ was found to be (perhaps fortuitously) indistinguishable from experimental results shown in Fig. 2.

These thermodynamic data are not affected by the non-stoicheiometry of cadmium oxide which is negligible in extent under the conditions studied; even with 1 atm. of cadmium vapour, the excess of metal amounts to only 0·5%.[6]

We thank Mr. J. Lumsden for helpful discussions, Dr. Azzam for preliminary experimental work, and the Imperial Smelting Corporation for a bursary (I. G. F. G.).

## Appendix

*Calculation, from thermodynamic data, of the free energy of the reaction :*

$$CdO\ (s) = Cd\ (g) + \tfrac{1}{2}O_2\ (g) \quad . \ . \ . \ . \ . \ . \ . \ . \ . \ . \quad (i)$$

The standard heat of the above reaction at 25° c (298·1° K), $\Delta H^\circ_{298}$, is obtained from Mah's value [5] for the reaction :

$$Cd\ (s) + \tfrac{1}{2}O_2\ (g) = CdO\ (s), \text{ namely, } \Delta H_{298} = -61{,}200\ (\pm 200)\ \text{cal.}$$

together with a value for the heat of sublimation, $\Delta H_{sub.}$ calculated from Egerton and Raleigh's vapour-pressure data.[7] Their results lead to $\Delta H_{sub.}$ at 500° K = 26,590. The specific heats of Cd (g) and Cd (s) are 4·97 and $(5{\cdot}31 + 2{\cdot}94 \times 10^{-3}T)$ respectively.[8] Hence, by Kirchhoff's equation, $\Delta H_{sub.}$ at 298° K is obtained as +26,900 cal, giving, for reaction (i)

$$\Delta H^\circ_{298} = +88{,}100\ \text{cal.}$$

The standard entropy of the reaction is obtained from the following absolute entropies at 298·1° K : for Cd (g), 40·07 ± 0·01 (Sackur's equation); for CdO (s), 13·1 ± 0·3 from Millar's low-temperature specific-heat determinations; [9] for $\frac{1}{2}O_2$ (g), 24·31 ± 0·01 (Kelley [8]). Hence, for reaction (i)

$$\Delta S^\circ_{298} = +51{\cdot}45 \pm 0{\cdot}3\ \text{cal. degree}^{-1}$$
$$\text{and}\quad \Delta G^\circ_{298} = +72{,}800\ \text{cal.}$$

To obtain a free-energy equation for a range of temperatures, use is made of the following specific heats : for CdO (s), $C_p = 9{\cdot}78 + 2{\cdot}02 \times 10^{-3}T$ (estimated by Kelley [8]); for $\frac{1}{2}O_2$, $C_p = 3{\cdot}58 + 0{\cdot}50 \times 10^{-3}T - 0{\cdot}20 \times 10^5T^{-2}$ (Kelley [8]); for Cd (g), $C_p = 4{\cdot}97$ (monatomic gas).

By standard methods, the final equation is obtained as

$$\Delta G_T^\circ = 88{,}465 + 1{\cdot}23T \ln T + 7{\cdot}6 \times 10^{-4}T^2 + 1{\cdot}0 \times 10^5T^{-1} - 59{\cdot}84T$$

The uncertainty in this equation probably does not exceed 1 kcal. at 1000° K.

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[*Received, April 4th, 1956.*]

[5] Mah, *J. Amer. Chem. Soc.*, 1955, **78**, 3363.
[6] Faivre, *Ann. Chim. France*, 1944, **19**, 58.
[7] Egerton and Raleigh, *J.*, 1923, **123**, 3024.
[8] Kelley, *U.S. Bur. Stand. Bull.*, 1949, No. 476; 1950, No. 477.
[9] Millar, *J. Amer. Chem. Soc.*, 1928, **50**, 2653.

## 761. *The Free Energy of Formation of Zinc Aluminate.*

By I. G. F. Gilbert and J. A. Kitchener.

The equilibrium

$$ZnAl_2O_4\ (s) + H_2\ (g) = Zn\ (g) + H_2O\ (g) + Al_2O_3\ (s)$$

has been investigated over the range 771—1044° c, and the results used to calculate the free energy of formation of zinc aluminate from the oxides. The forms of alumina involved have been studied and are discussed.

In a previous paper [1] determination of the equilibrium constants of the reactions

$$ZnO\ (s) + H_2\ (g) = Zn\ (g) + H_2O\ (g) \quad . \ . \ . \ . \ . \ . \quad (1)$$

and

$$Zn_2SiO_4\ (s) + H_2\ (g) = 2Zn\ (g) + H_2O\ (g) + SiO_2\ (s) \quad . \ . \ . \quad (2)$$

was described, and hence the free energy of formation of zinc silicate from zinc oxide and silica was derived. In the present paper similar equilibrium measurements are reported for the reaction

$$ZnAl_2O_4\ (s) + H_2\ (g) = Zn\ (g) + H_2O\ (g) + Al_2O_3\ (s) \quad . \ . \ . \quad (3)$$

These results are combined with the data already obtained for reaction (1) to obtain the free energy of formation of zinc aluminate.

In order to define the composition of the solid phase (which might conceivably be non-stoicheiometric) the equilibrium was established in the presence of excess of α-aluminium oxide.

### Experimental

The furnace, measurement of temperature, and technique were similar to those described previously,[1] except that the furnace contained a closely fitting alumina tube to eliminate silica from the reaction zone.

Zinc aluminate was prepared by ignition of the co-precipitated zinc hydroxide and (excess of) aluminium hydroxide at 1100° c for several hours. *X*-Ray powder diagrams of the product showed the presence of alumina and zinc aluminate only. Preparations at 1050° c (the experimental maximum) of nominal composition from 33% to 72% of $Al_2O_3$ had the same lattice parameter to within about 1 part in 8000 parts, indicating the absence of appreciable non-stoicheiometry.

Two gas streams were used in these experiments : one of " oxygen-free " nitrogen and one of cylinder " forming-gas " ($H_2$ 25%, $N_2$ 75%), freed from oxygen by passage over heated palladized asbestos. Both gases were dried by anhydrous magnesium perchlorate.

The hydrogen–nitrogen mixture was analysed by burning a measured volume over heated

| Temp. (c) | $p_{Zn}$ ($10^{-3}$ atm.) | $-\log_{10} K$ (atm.) | Flow rate (c.c./min.) | Temp. (c) | $p_{Zn}$ ($10^{-3}$ atm.) | $-\log_{10} K$ (atm.) | Flow rate (c.c./min.) |
|---|---|---|---|---|---|---|---|
| 771° | 0·517 | 5·985 | 56 | 906 | 3·56 | 4·299 | 67 |
| 787 | 0·656 | 5·774 | 68 | 969 | 7·51 | 3·656 | 31 |
| 791 | 0·716 | 5·700 | 110 | 970 | 7·71 | 3·632 | 52 |
| 792 | 0·771 | 5·634 | 60 | 973 | 7·85 | 3·615 | 68 |
| 873 | 2·16 | 4·733 | 48 | 1041 | 16·17 | 2·969 | 55 |
| 874 | 2·13 | 4·746 | 78 | 1044 | 16·34 | 2·959 | 76 |
| 874 | 2·24 | 4·701 | 64 | 1044 | 15·71 | 2·940 | 92 |
| 905 | 3·31 | 4·362 | 62 | | | | |

copper oxide and collecting and weighing the water produced in anhydrous magnesium perchlorate. The cylinder of gas used contained 0·2592 ± 0·0015 mole of hydrogen per mole of mixture. The volume of gas passed through the condenser was measured with a wet gas meter.[2]

The zinc condensed was determined gravimetrically as zinc ammonium phosphate.

The experimental procedure was similar to that previously described,[2] a stream of nitrogen

[1] Kitchener and Ignatowicz, *Trans. Faraday Soc.*, 1951, **47**, 1278.
[2] Gilbert and Kitchener, preceding paper.

being used in the preparatory period, followed by one of a hydrogen–nitrogen mixture. A correction was found by a separate experiment. In no example was this more than a few units %, and at the lower temperatures it was negligible.

*Results.*—The method of calculation was similar to that used in the example of zinc silicate.[1] The results are given in the Table. The graph of log $K$ against $1/T$ is accurately linear (see

$$ZnAl_2O_4\,(s) + H_2\,(g) = Zn\,(g) + H_2O\,(g) + Al_2O_3\,(s).$$

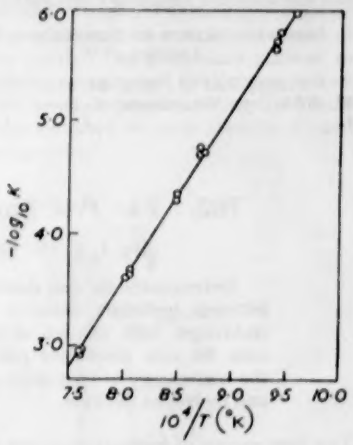


Figure), and there is no systematic dependence on flow rate; this shows that errors due to failure to saturate the entraining gas and thermal diffusion have been eliminated.

The best straight line representing the results was found by the method of least squares to be :

$$\log_{10} K\ (\text{atm.}) = 8{\cdot}622 - 15{,}253/T$$

## Discussion

The standard Gibbs free energy of reaction (3) follows from the equation above :

$$\Delta G^\circ\ (\text{at } 1060\text{—}1317^\circ\text{ K})\ (\pm 70^\circ) = 69{,}760\ (\pm 1600) - 39{\cdot}44\ (\pm 1{\cdot}3)T\ \text{cal./mole.}$$

On combination with the corresponding equation for (1), there follows for

$$ZnO\,(s) + Al_2O_3\,(s) = ZnAl_2O_4\,(s) \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$\Delta G^\circ\ (\text{at } 1060\text{—}1317^\circ\text{ K})\ (\pm 80^\circ) = -14{,}120\ (\pm 1700) + 1{\cdot}17\ (\pm 1{\cdot}3)T$$

There is some uncertainty regarding the allotropic form of the alumina which enters into reactions (3) and (4). On the one hand, the products of almost complete reduction of zinc aluminate, as found in separate experiments, consist of $\gamma$- and $\theta$-alumina, depending on the temperature. Fricke and Weitbrecht [3] found $\gamma$-aluminas as a product of complete reduction of nickel aluminate in a similar temperature range. The particle size in this example was small enough to influence the free energy, but Richardson and Jeffes [4] have suggested that this is due to the simultaneous formation of two solid products which mutually interfere with crystal growth.

On the other hand, the technique used in the present work employs a large amount of reactant relative to the amount of reduction, and consequently small amounts of " active " alumina would probably dissolve in the spinel saturated by the stable form, and would have little influence on the free energy of the phases. In agreement with this, only $\alpha$-alumina could be detected by $X$-ray analysis of the material after the equilibrium

[3] Fricke and Weitbrecht, *Z. Elektrochem.*, 1942, **48**, 86.
[4] Richardson and Jeffes, *J. Iron Steel Inst.*, 1948, **160**, 261.

experiments, and no deviations from linearity, corresponding to phase changes $\gamma$-$Al_2O_3$ $\longrightarrow$ $\theta$-$Al_2O_3$ $\longrightarrow$ $\alpha$-$Al_2O_3$, are apparent in the graph. The thermodynamic properties of the various forms of alumina are as yet little elucidated.[5]

We thank Mr. J. Lumsden for helpful discussions and the provision of the *X*-ray analyses, and the Imperial Smelting Corporation for a bursary (to I. G. F. G.).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7. [*Received, April 4th*, 1956.]

[5] Fricke, *Koll. Z.*, 1934, **69**, 312; Stumpf, Russell, Newsome, and Tucker, *Ind. Eng. Chem.*, 1950, **42**, 1398; von Wartenberg, *Z. anorg. Chem.*, 1952, **269**, 76; Schneider and Gattow, *ibid.*, 1954, **277**, 41.

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## 762. *The Free Energy of Formation of Zinc Ferrite.*

By I. G. F. GILBERT and J. A. KITCHENER.

Determinations are described of the equilibria at high temperatures between hydrogen chloride and (*a*) zinc aluminate and (*b*) zinc ferrite (saturated with respect to ferric oxide). By combining the results with data for zinc aluminate previously determined, there result equations for the free energy of formation of zinc ferrite and for the reaction of zinc oxide and hydrogen chloride.

THE free energy of formation of zinc ferrite

$$ZnO\ (s) + Fe_2O_3\ (s) = ZnFe_2O_4\ (s) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

cannot conveniently be derived from determinations of hydrogen-reduction equilibria (as previously used for zinc aluminate) because of the high oxygen potential of ferric oxide and the complete miscibility of the ferrite and its first reduction product (*i.e.*, $Fe_3O_4$) at high temperatures.[1] The method finally adopted was to combine measurements of the equilibria with hydrogen chloride,

$$ZnFe_2O_4\ (s) + 2HCl\ (g) = ZnCl_2\ (g) + H_2O\ (g) + Fe_2O_3\ (s) \quad . \quad . \quad (2)$$

$$ZnAl_2O_4\ (s) + 2HCl\ (g) = ZnCl_2\ (g) + H_2O\ (g) + Al_2O_3\ (s) \quad . \quad . \quad (3)$$

with the data previously obtained for

$$ZnO\ (s) + Al_2O_3\ (s) = ZnAl_2O_4\ (s) \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The spinel phase in the system ZnO–$Fe_2O_3$ has a large range of composition;[2] no attempt has been made to investigate the whole range, but only that at the $Fe_2O_3$ edge as defined by the presence of excess of this oxide.

There are a number of possible side reactions which might interfere with the investigation of reactions (2) and (3). However, preliminary calculations from available thermodynamic and other data showed that they would not interfere under the conditions studied. In particular, the reactions of hydrogen chloride with alumina, with ferric oxide, and with the oxygen derived from its dissociation are negligible in the experimental conditions, and solid oxychlorides of zinc and of iron are not formed.

### EXPERIMENTAL

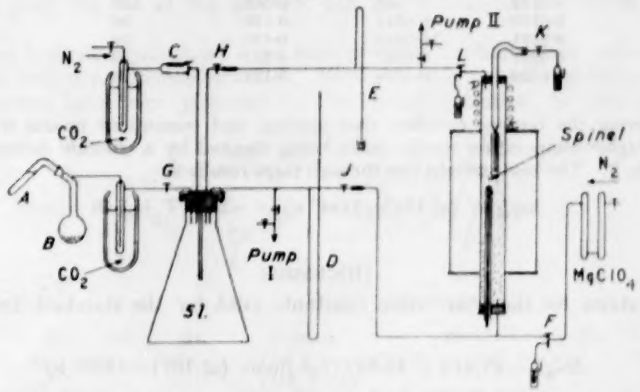
The apparatus is shown in the Figure. Hydrogen chloride was prepared by tilting a controlled amount of concentrated sulphuric acid from tube *A* on to solid ammonium chloride ("AnalaR," previously dried at 110°) in flask *B*, and entered the 5-l. reservoir through a solid carbon dioxide trap. The diluent, cylinder nitrogen, was dried in the same way. Pressures

[1] Mason, *Amer. Mineral*, 1947, **32**, 426.
[2] Berger, *Festskr. J. Arvid Hedvall*, 1948, p. 31.

in the reservoir system were measured by manometer *D*, and in the furnace system by manometer *E*. Stopcocks were held in place by wire clips, and the lubricants were first shown to be inappreciably attacked by hydrogen chloride. The volume of the reservoir was obtained by gas dilution from a smaller bulb of directly measured capacity. Zinc aluminate was prepared as in the preceding paper, and zinc ferrite similarly from " AnalaR " zinc oxide and pure iron.

The furnace was brought to a steady temperature, with a stream of dry nitrogen entering through *F*. The reservoir system was evacuated, and a measured pressure of hydrogen chloride introduced, after which nitrogen was allowed to enter through *C* to give a measured excess of pressure of about 1 atm. Temperature corrections were made. The gases were allowed to mix. The condenser was sealed in position with de Khotinsky cement, and the furnace system evacuated. Mixed gas then entered through *H* and *L*, this arrangement eliminating the blank, after which the nitrogen–hydrogen chloride gas stream was switched to enter through *F*, and

HCl *apparatus.*




out through *L*, for time to allow steady conditions to be reached; thereafter the entire flow of a measured pressure of gas was passed through the condenser. To ensure complete deposition of zinc chloride, and also of hydrogen chloride, a tube of moist glass-wool and a silver nitrate bubbler were placed on the outlet side.

Chloride and zinc in the dissolved condensate were determined gravimetrically as AgCl and $ZnNH_4PO_4$, respectively.

*Results.*—The equilibrium constant is

$$K = p_{ZnCl_2}.p_{H_2O}/p_{HCl}^2$$

and by the ideal-gas laws,

$$p_{ZnCl_2} = \frac{w(P + p)R}{65{\cdot}4V(P_1/T_1 - P_2/T_2)}$$

where $w$ (g.) = mass of zinc condensed, $V$ (l.) = volume of reservoir, $P$ = atmospheric pressure, $p$ = the excess of pressure in the furnace, $P_1$, $P_2$ are the initial and final pressures in the reservoir, and $T_1$, $T_2$ the initial and final temperatures of the reservoir.

By the stoicheiometry of the reaction $p_{ZnCl_2} = p_{H_2O}$.

1. *Zinc aluminate* ($ZnAl_2O_4$). The results for the hydrogen chloride equilibrium are given in Table 1. There is no systematic dependence on flow rate and therefore a true equilibrium had been reached and measured.

TABLE 1.

| Temp. (c) | $p_{ZnCl_2}$ (atm. $\times 10^{-2}$) | $p_{HCl}$ (initial) (atm.) | $-\log_{10} K$ (atm.) | Mean flow rate (c.c./min.) | Temp. (c) | $p_{ZnCl_2}$ (atm. $\times 10^{-2}$) | $p_{HCl}$ (initial) (atm.) | $-\log_{10} K$ (atm.) | Mean flow rate (c.c./min.) |
|---|---|---|---|---|---|---|---|---|---|
| 798° | 0·912 | 0·1309 | 2·184 | 110 | 872° | 1·138 | 0·1087 | 1·756 | 70 |
| 807 | 0·658 | 0·0770 | 1·973 | 40 | 952 | 1·309 | 0·0903 | 1·380 | 50 |
| 810 | 1·268 | 0·1786 | 2·164 | 30 | 953 | 0·907 | 0·0688 | 1·495 | 40 |
| 846 | 0·402 | 0·0447 | 1·921 | 60 | 1034 | 1·031 | 0·0596 | 1·156 | 30 |
| 857 | 1·316 | 0·1242 | 1·744 | 50 | 1036 | 1·306 | 0·0684 | 1·021 | 60 |
| 871 | 1·246 | 0·1160 | 1·728 | 50 | 1037 | 1·511 | 0·0873 | 1·155 | 50 |

By the method of least squares the best straight line through these points is found to be :

$$\log_{10} K \text{ (at 1071—1310° K)} = 3{\cdot}471 - 5992/T \ (\pm 0{\cdot}067).$$

2. *Zinc ferrite* ($ZnFe_2O_4$). The results obtained in the same temperature range were irreproducible, and further investigation showed that chloride was being taken up within the furnace. The cause of this reaction could not be ascertained. Further experiments were made at a range of higher temperatures (for which the original nichrome furnace winding was replaced with one of " Kanthal "). At temperatures of 1100° c and above, it was found that the total

TABLE 2.

| Temp. (K) | $p_{ZnCl_2}$ | $p_{HCl}$ | $-\log_{10} K$ | Recovery of $Cl^-$ (%) | Mean flow rate (c.c./min.) |
|---|---|---|---|---|---|
| 1418° | 0·0204 | 0·0560 | 0·254 | 107 | 30 |
| 1424 | 0·0192 | 0·0558 | 0·086 | 106 | 30 |
| 1367 | 0·0190 | 0·0541 | 0·139 | 98 | 40 |
| 1367 | 0·0191 | 0·0548 | 0·120 | 98 | 30 |
| 1484 | 0·0207 | 0·0557 | 0·322 | 99 | 45 |
| 1481 | 0·0190 | 0·0544 | 0·128 | 99 | 60 |

chloride entering the furnace equalled that leaving, and concordant results were obtained. Only these higher-temperature results (each being checked by a chloride determination) are given in Table 2. The best straight line through these results is

$$\log_{10} K \text{ (at 1367—1484° K)} = -2000/T + 1{\cdot}58$$

## DISCUSSION

The equations for the equilibrium constants yield for the standard free energy of reaction (3) :

$$\Delta G_3^\circ = 27{,}410 - 15{\cdot}88T \text{ cal./mole (at 1071—1310° K)}$$

and for reaction (2) :

$$\Delta G_2^\circ = 9150 - 7{\cdot}23T \text{ cal./mole (at 1367—1484° K)}$$

On combination of these with the earlier value [3] for reaction (4), there results for reaction (1), after averaging because of the uncertainty in the slope :

$$\Delta G_4^\circ = -6490 \text{ cal./mole ZnO (at 1367—1484° K)}$$

This is considered the best representation of the results. The experimental results also yield a direct value for the free energy of the reaction between hydrogen chloride and zinc oxide at high temperatures,

$$ZnO\ (s) + 2HCl\ (g) = ZnCl_2\ (g) + H_2O\ (g) \quad . \ . \ . \ . \quad (5)$$

by combining the equations for reactions (3) and (4) :

$$\Delta G_5^\circ = +13{,}290 - 14{\cdot}71T \text{ cal./mole (at 1071—1310° K)}$$

We thank Mr. J. Lumsden for helpful discussions and the Imperial Smelting Corporation for a bursary (to I. G. F. G.).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.7.

[*Received, April 4th*, 1956.]

[3] Gilbert and Kitchener, preceding paper.

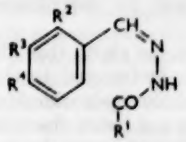
## 763. *Phthalazines. Part I. Re-investigation of the Preparation of Phthalazines by Cyclodehydration of Acylhydrazones.*

By H. J. Rodda and P. E. Rogasch.

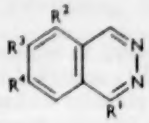
The preparation of substituted phthalazines by Aggarwal's method,[3,4] involving cyclodehydration of acylhydrazones, has been critically examined. This method does not in fact lead to the formation of phthalazines; the products are azines resulting from fragmentation of the starting materials.

As part of an investigation of phthalazines we have been interested in the preparation of 1-alkyl- and 1-aryl-phthalazines. Difficulties associated with the preparation of *o*-formylaryl ketones, which could be condensed with hydrazine or substituted hydrazines to yield phthalazines, limit the use of this method, and two alternative procedures have been developed.

The known 1-alkylphthalazines [1] have been prepared exclusively by reduction of the corresponding 1-alkyl-4-chlorophthalazines. With the exception of 1-phenylphthalazine,[2] 1-arylphthalazines have been prepared by the cyclodehydration, in acid medium, of



(I — XI)



(Ia — XIa)

| Formula | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| I, Ia | Ph | H | H | H |
| II, IIa | ,, | ,, | ,, | MeO |
| III, IIIa | ,, | MeO | ,, | H |
| IV, IVa | ,, | H | MeO | MeO |
| V, Va | ,, | ,, | O·$CH_2$·O | |
| VI, VIa | $CH_2Ph$ | ,, | H | MeO |

| Formula | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| VII, VIIa | $CH_2Ph$ | H | MeO | MeO |
| VIII, VIIIa | ,, | ,, | O·$CH_2$·O | |
| IX, IXa | 3 : 4-$(MeO)_2C_6H_3$·$CH_2$· | ,, | MeO | MeO |
| X, Xa | 3 : 4-$(MeO)_2C_6H_3$· | ,, | ,, | ,, |
| XI, XIa | 3 : 4-$CH_2$<$O_2$>$C_6H_3$· | ,, | O·$CH_2$·O | |

acylhydrazones by Aggarwal's method.[3,4] Thus the acylhydrazones (I—IX) were reported to yield the phthalazines (Ia—IXa), respectively. In the only independent application of the method, Wilson [5] reported the successful preparation of 1-(3 : 4-dimethoxyphenyl)-6 : 7-dimethoxyphthalazine (X) and 6 : 7-methylenedioxy-1-(3 : 4-methylenedioxyphenyl)-phthalazine (IXa) from (X) and (XI), respectively. It has now been shown that the procedure does not in fact lead to phthalazines.

As a modification of Aggarwal's method, which involves pentyl alcohol–hydrochloric acid as cyclodehydrating reagent, polyphosphoric acid was used in an attempt to cyclise *o*-nitro- and *m*-nitro-benzaldehyde benzoylhydrazone. The products isolated were *o*-nitro- and *m*-nitrobenzaldazines resulting from hydrolysis of the acylhydrazone and subsequent reaction of the hydrolysis products; we were unable to detect phthalazines in the reaction products. The same compounds resulted when either pentyl alcohol–hydrochloric acid or phosphoric oxide in xylene was used to effect ring-closure, and we were led to re-examine the compounds prepared by Aggarwal *et al.* and by Wilson. One pecularity was immediately apparent; the compounds (IVa), (VIIa), (IXa), (Xa), described as phthalazines and resulting from various 3 : 4-dimethoxybenzaldehyde acylhydrazones, were all recorded as having m. p. within the range 191—194°; 3 : 4 : 3′ : 4′-tetramethoxybenzaldazine [6] has

[1] Simpson, "The Chemistry of Heterocyclic Compounds," Interscience Publishers, Ltd., London, 1953, Vol. 5, p. 72.
[2] Lieck, *Ber.*, 1905, **38**, 3918.
[3] Aggarwal, Darbari, and Ray, *J.*, 1929, 1941.
[4] Aggarwal, das Khera, and Ray, *J.*, 1930, 2354.
[5] Wilson, *J. Amer. Chem. Soc.*, 1948, **70**, 1901.
[6] Vorlander, *Ber.*, 1906, **39**, 809.

m. p. 191°. The so-called phthalazines (Va), (VIIIa), and (XIa), derived from piperonaldehyde acylhydrazones, had m. p. 200—204°; piperonaldazine [6] has m. p. 203°. Similarly, the compounds to which structures (IIa) and (VIa) had been assigned had m. p. 167° and 168—169°, respectively, which are in good agreement with m. p. 168° of 4 : 4′-dimethoxybenzaldazine.[7]

We have repeated the reaction of these acylhydrazones with pentyl alcohol–hydrochloric acid and with polyphosphoric acid and have shown that in each case the product is the azine, identified by m. p. and mixed m. p. with authentic specimens.

The physical constants ascribed by Aggarwal to compounds (Ia) (m. p. 174—175°) and (IIIa) (m. p. 135°) do not agree with the literature values for benzaldazine [8] (m. p. 93°), and 2 : 2′-dimethoxybenzaldazine [6] (m. p. 143°) but in our hands the azines have been obtained. It is significant that 1-phenylphthalazine, prepared by the reductive dehalogenation of 4-chloro-1-phenylphthalazine [2] is described as having m. p. 142—143°.

The formation of azines under the conditions used by Aggarwal is probably the result of alcoholysis with simultaneous formation of pentyl esters, for when polyphosphoric acid [10 g. of phosphoric oxide in 10 c.c. (85%, *d* 1·75) of phosphoric acid] was used all the *N*-benzoylhydrazones gave benzoic acid as a by-product. When the proportion of phosphoric oxide was increased the reaction was metathetical, the azine being accompanied by 2 : 5-diphenyl-1 : 3 : 4-oxadiazole, presumably formed by dehydration of the intermediary *NN*-dibenzoylhydrazine.

It was therefore necessary to reinvestigate the claim that the products of cyclisation of the acylhydrazones (VI) and (VIII) were hydrolysed to the corresponding 2-acetylphenylbenzaldehydes by phthalic acid in alcoholic hydrochloric acid,[4] for it is impossible for such products to arise from the azines. In our hands the azines were partially decomposed to the parent aldehyde when digested with alcoholic hydrochloric acid–phthalic acid and indeed the m. p. quoted [4] for 4-methoxy- and 3 : 4-methylenedioxy-2-phenylacetylbenzaldehyde bisphenylhydrazones (122° and 104°, respectively) correspond to the literature values for the phenylhydrazones of anisaldehyde (120—121°) and piperonaldehyde (103°).

Exploratory experiments have indicated that 1-alkyl- and 1-aryl-phthalazines can be prepared readily by hydrolysis of the corresponding toluene-*p*-sulphonylhydrazine derivatives;[9,10] the results of this study will be published subsequently.

## Experimental

*Attempted Cyclodehydration of Acylhydrazones.*—*o*-Nitrobenzaldehyde benzoylhydrazone (1 g.) was heated for 6 hr. at 130—140° in polyphosphoric acid [10 g. of phosphoric oxide in 10 c.c. of phosphoric acid (*d* 1·175)], the mixture was poured into water (400 c.c.), and the aqueous suspension warmed for 30 min. The product was washed, dried, and crystallised from alcohol; it formed pale yellow crystals (0·5 g.), m. p. 209° undepressed by authentic 2 : 2′-dinitrobenzaldazine (Found: C, 56·4; H, 3·4; N, 18·3. 5-Nitro-1-phenylphthalazine, $C_{14}H_9O_2N_3$, requires C, 66·9; H, 3·6; N, 16·7. 2 : 2′-Dinitrobenzaldazine, $C_{14}H_{10}O_4N_4$, requires C, 56·4; H, 3·4; N, 18·8%). The same product was formed when *o*-nitrobenzaldehyde benzoylhydrazone was refluxed with anhydrous pentyl alcohol–hydrochloric acid or with phosphoric oxide in xylene.

Similarly *m*-nitrobenzaldehyde benzoylhydrazone yielded 3 : 3′-dinitrobenzaldazine, m. p. and mixed m. p. 198° (Found: C, 56·4; H, 3·4; N, 18·4. 6-Nitro-1-phenylphthalazine, $C_{14}H_9O_2N_3$, requires C, 66·9; H, 3·6; N, 16·7. 3 : 3′-Dinitrobenzaldazine requires C, 56·4; H, 3·4; N, 18·8%). The acylhydrazones (IV), (VII), and (IX) yielded 3 : 4 : 3′ : 4′-tetramethoxybenzaldazine, m. p. and mixed m. p. 190—191°, and the hydrazones (V) and (VII), on treatment with any of the cyclodehydrating agents cited above, gave piperonaldazine, m. p. 203°. The compounds (II) and (VI) yielded 4 : 4′-dimethoxybenzaldazine, m. p. 168°.

Whenever benzoylhydrazones were treated with polyphosphoric acid small quantities of

[7] Knopfer, *Monatsh.*, 1909, **30**, 31.
[8] Curtius and Jay, *J. prakt. Chem.*, 1889, **39**, 44.
[9] Albert and Royer, *J.*, 1949, 1148.
[10] Osborn and Schofield, *J.*, 1955, 2102.

benzoic acid were isolated. When the proportion of phosphoric oxide in the polyphosphoric acid was doubled there resulted 2 : 5-diphenyl-1 : 3 : 4-oxadiazole, m. p. and mixed m. p. 139°.

*Hydrolysis.*—4 : 4′-Dimethoxybenzaldazine (0·5 g.) and phthalic acid (0·5 g.) were refluxed in alcoholic hydrochloric acid (15 c.c.) for 8 hr. When the mixture cooled a small quantity of white crystals (phthalhydrazide?) was deposited. The clarified solution was worked up according to Aggarwal[4] and the resulting material converted into the 2 : 4-dinitrophenylhydrazone. The product, crystallised from alcohol, had m. p. 249°, undepressed by an authentic specimen of *p*-methoxybenzaldehyde 2 : 4-dinitrophenylhydrazone.

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## 764. *The Thermal Degradation of Polymethacrylonitrile. Part I. Separation of Coloration and Depolymerization Reactions.*

By N. GRASSIE and I. C. MCNEILL.

The colour which develops in polymethacrylonitrile at 120° is due to a reaction initiated at impurities in the polymer chains. These are eliminated by suitable purification of the monomer and by carrying out the polymerization in a vacuum in presence of αα′-azo*iso*butyronitrile as catalyst.

By using such polymers the depolymerization reaction, which occurs at 220° and affords quantitative yields of monomer, can be investigated in absence of the complications due to coloration.

The coloration reaction is most conveniently studied in copolymers of methacrylonitrile with traces of methacrylic acid. The methacrylic acid units act as centres of initiation, the concentration of which can be closely controlled in the preparation of the material.

SINCE polymethacrylonitrile is derived from a 1 : 1-disubstituted monomer it would be expected, like poly(methyl methacrylate), poly-α-methylstyrene, poly(vinylidene cyanide), etc., to be capable of decomposing quantitatively to monomer.[1] Appreciable yields of monomer can indeed be obtained thermally from polymethacrylonitrile although these have never approached 100%.[2] Simultaneously the polymer develops colour and becomes insoluble. The principal features of this coloration reaction prove it to be quite unusual and of considerable chemical interest. Superficially it appears to be similar to the coloration produced in solution by alkali.[3] This paper describes some preliminary experiments which define the conditions under which the depolymerization and coloration reactions take place and shows how they can be separated for individual study.

*Results and Discussion.*—When the temperature of a methacrylonitrile polymer which is liable to develop colour is slowly raised in a vacuum, the following general behaviour is observed. At 110° the polymer remains clear and colourless but has softened to such an extent that volatile material readily escapes. Above 120° the material rapidly changes colour through yellow, orange, and red to deep red. Simultaneously it gradually becomes insoluble and infusible. No further appreciable evolution of volatile material is discernible till monomer is evolved at approximately 220°. Fig. 1 shows how the rate of evolution of volatile material varies as the temperature of such a polymer sample is slowly raised to 270° in the dynamic molecular still.[4]

While the coloration of polymethacrylonitrile has always been regarded as characteristic of the polymer, it was quite clear that the ease and extent of coloration were liable to vary widely from sample to sample. Investigation of the factors involved proves that the method of purification of the monomer, the nature of the catalyst, and the method of polymerization may all have an effect as shown in Table 1.

[1] Grassie, "The Chemistry of High Polymer Degradation Processes," Butterworths Scientific Publications Ltd., London, 1956, Chapters 1 and 2.
[2] Kern and Fernow, *J. prakt. Chem.*, 1942, **160**, 296.
[3] McCartney, U.S. Nat. Bur. Stand. Circ. No. 525, 1953, p. 123.
[4] Grassie and Melville, *Proc. Roy. Soc.*, 1949, *A*, **199**, 1; Grassie, *Trans. Faraday Soc.*, 1952, **48**, 379.

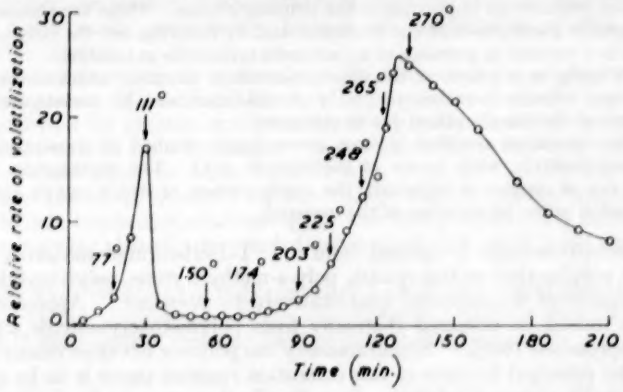


FIG. 3. *Infrared spectra of polymers A—D in Table* 1 *and a copolymer of methacrylonitrile with traces*

It is also quite clear that the tendency for polymer to develop colour is closely linked with the ultimate yield of monomer which can be obtained at high temperatures; *e.g.*, when the polymer referred to in Fig. 1 (which colours readily) is heated rapidly to 310°, yields of only 58% are produced, but this is reduced to 52% when the colour is first increased by preheating to 160° for 30 min. On the other hand, polymer D (Table 1) is converted almost quantitatively into monomer under the same conditions. Thus when coloration is eliminated the material behaves precisely as one would predict by comparison with other polymers derived from 1 : 1-disubstituted monomers.

The data in Table 1 suggest that the ease of coloration may be associated in some way with the presence of impurities. The infrared spectra of the polymers in Table 1 are shown in Fig. 2 (*A*—*D*). The main difference between them resides in the band at 1720 cm.$^{-1}$, the intensity of which runs closely parallel to the ease of coloration of the polymers at high temperatures. The region of this band, the fact that it can be eliminated by washing the monomer with alkali, the obvious possibility of cyanide groups'

FIG. 1. *Rate of evolution of volatile material from polymethacrylonitrile which becomes coloured (copolymer of methacrylonitrile with traces of methacrylic acid).*




being converted into carboxyl, and the fact that reprecipitation of the polymers affects neither the intensity of the band nor the coloration properties, all suggest that the 1720 cm.$^{-1}$ band is due to carbonyl groups incorporated in one way or another into the molecular chains. It is therefore concluded that structures involving carbonyl groups act as centres of initiation for the coloration reaction.

TABLE 1. *Factors involved in the coloration of polymethacrylonitrile.*

| Polymer preparation | Coloration at 160° |
|---|---|
| A. Monomer purified by distillation (Method *a*) | Rapid |
| Monomer purified by washing with alkali (Method *b*) : | |
| B. Polymerized in air | Rapid |
| C. Polymerized *in vacuo* with benzoyl peroxide as catalyst | Slight |
| D. Polymerized *in vacuo* with αα′-azo*iso*butyronitrile as catalyst | None |

Beaman reported a strong peak at 1710 cm.$^{-1}$ in the infrared spectrum of polymethacrylonitrile prepared by anionic catalysis and he attributed this to residual acetone in the polymer film.[5] This cannot be the explanation in the polymers under discussion, however, since reprecipitation does not affect the coloration properties.

Strause and Dyer [6] have shown that oxygen readily copolymerizes with methacrylonitrile. Primarily, peroxidic structures are undoubtedly formed. Being labile, however,

[5] Beaman, *J. Amer. Chem. Soc.*, 1948, **70**, 3115.
[6] Strause and Dyer, *ibid.*, 1956, **78**, 136.

FIG. 2. *Infrared spectra of polymers A—D in Table 1 and a copolymer of methacrylonitrile with traces of methacrylic acid (E).*

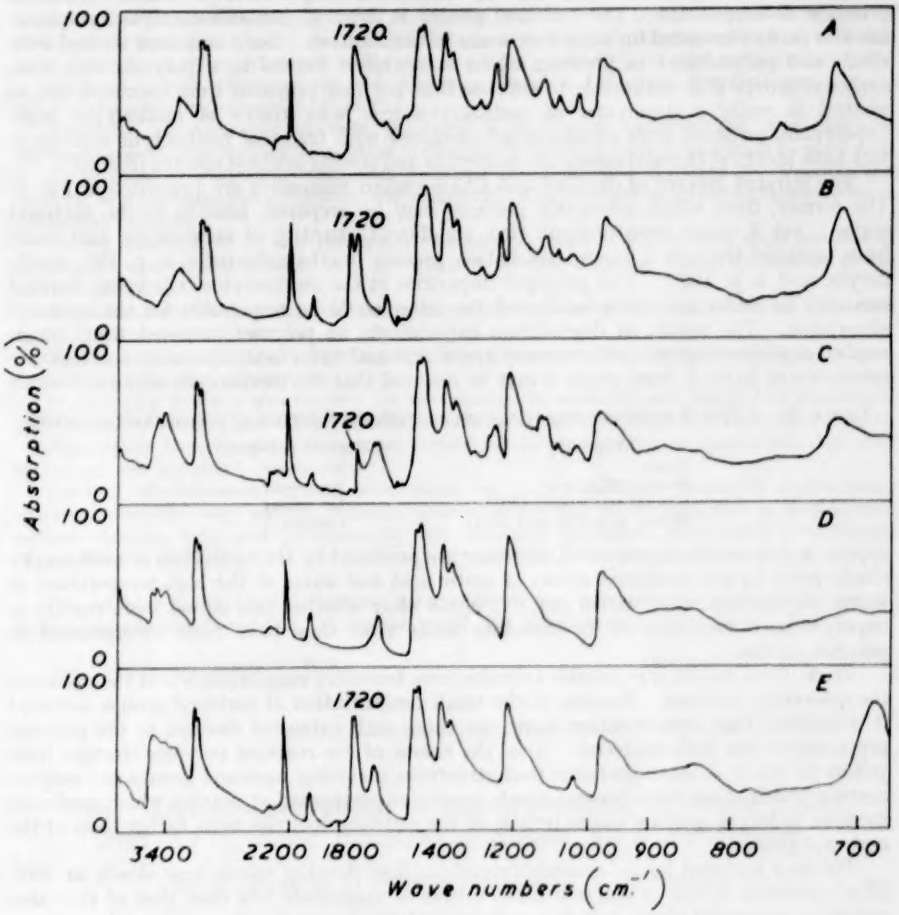
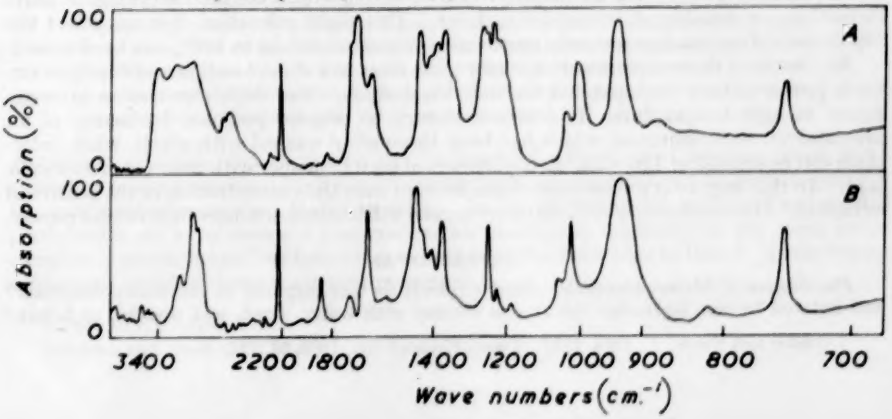



FIG. 3. *Infrared spectra of distilled (A) and alkali-washed (B) monomers.*



these will decompose to produce other oxygenated structures including carbonyl groups. The double carbonyl peak in Fig. 2*B* is probably due to products of different modes of peroxide decomposition. The carbonyl groups in benzoyl peroxide-catalysed polymers are also easily accounted for since they occur in the catalyst. Since monomer washed with alkali and polymerized in presence of an azo-catalyst results in a polymer free from carbonyl groups it is reasonable to suppose that polymer prepared from monomer not so washed is really a copolymer of methacrylonitrile with traces of methacrylic acid. Copolymers prepared from alkali-washed monomer with traces of methacrylic acid do in fact have identical thermal coloration properties and similar infrared spectra (Fig. 2*E*).

The infrared spectra of distilled and alkali-washed monomers are presented in Fig. 3. The former, from which colourable polymer may be prepared, absorbs in the carbonyl region; yet it seems most unlikely that a sufficient quantity of methacrylic acid could have persisted through a careful distillation process (methacrylonitrile, b. p. 89°; methacrylic acid, b. p. 163°). The principal impurities in the methacrylonitrile being distilled can only be water and acetic acid, and the latter could be responsible for the carbonyl absorption. The results of degradation experiments on polymer prepared from alkali-washed monomer together with traces of acetic acid and water both separately and together are shown in Table 2, from which it may be deduced that the methacrylic acid units which

TABLE 2. *Effect of monomer impurities on coloration properties of polymethacrylonitrile.*

| Impurity | Effect on polymer |
|---|---|
| None | No colour |
| Water (5%) | No colour |
| Glacial acetic acid (5%) | No colour |
| Water + acetic acid (5%) | Colours |

appear in polymer from unwashed monomer are produced by the hydrolysis of methacrylonitrile units by the combined action of acetic acid and water at the high temperature at which polymerization is carried out. It is not clear whether this occurs more readily in unpolymerized monomer or in monomer units after they have been incorporated in polymer chains.

From these results it is possible to make some tentative suggestions about the nature of the coloration reaction. Because of the small concentration of carbonyl groups involved it is unlikely that their reaction alone can cause such extensive changes in the physical properties of the bulk material. Since the colour of the reacting polymer changes from yellow to red it is more probable that structures involving carbonyl groups act only as centres of initiation for a process which results in conjugated structures which gradually increase in length and are characteristic of the methacrylonitrile units rather than of the carbonyl groups.

Polymer initiated by $\alpha\alpha'$-azo*iso*butyronitrile does develop colour very slowly at 250°. This represents a rate of reaction many orders of magnitude less than that of the other polymers mentioned above. It does not appear to be the result of impurity in the polymer and is probably due to some initiation process occurring within the methacrylonitrile units themselves, or possibly at terminal structures. This slight coloration does not affect the depolymerization reaction seriously since yields of monomer close to 100% can be obtained.

As a result of these experiments it is now quite clear how the coloration and depolymerization processes may be separated for individual study. For depolymerization investigations at high temperatures it is only necessary to prepare polymer, by means of an azo-catalyst, from monomer which has been thoroughly washed with alkali, while coloration can be studied at 120—150° in copolymers of such monomer with traces of methacrylic acid. In this way a very close control can be kept over the concentration of the centres of initiation. The mechanisms of these two processes will be discussed more fully in later papers.

## EXPERIMENTAL

*Preparation of Methacrylonitrile.*—Methacrylonitrile was prepared as previously described [7] and isolated by two methods. (*a*) It was washed with water, dried, and distilled as before [7]

[7] Grassie and Vance, *J.*, 1954, 2122; *Trans. Faraday Soc.*, 1956, **52**, 727.

(b. p. 91—93°; yield 60% on acetone cyanohydrin). (*b*) Ammonia solution (*d* 0·88) was added with vigorous stirring to the pyrolysis mixture in a separating funnel until the lower, aqueous layer become alkaline to litmus. After separation, the monomer layer was washed repeatedly with water, dried ($CaCl_2$), and twice distilled (b. p. 89—90°). Further quantities of monomer were obtained by ether extraction of the aqueous layer (yield 50% on acetone cyanohydrin).

*Methacrylic acid.* Methacrylic acid (Imperial Chemical Industries Limited) was distilled once at atmospheric pressure (b. p. 163°).

*Catalysts.* αα'-Azo*iso*butyronitrile (Eastman Kodak) was recrystallized from toluene. Benzoyl peroxide was purified by solution in chloroform followed by reprecipitation by methanol.

*Preparation of Polymers.*—Monomer prepared as above was degassed by freezing and thawing in a vacuum, twice distilled, and sealed off under vacuum in Pyrex dilatometer tubes containing catalyst.

In the preparation of the copolymer, methacrylic acid (2·5% of the total volume of monomers) was poured directly into the dilatometer and degassed before distillation of the methacrylonitrile.

Approximately 0·7% of catalyst was used in each case and polymerizations were continued to 5—10% conversion at 65°.

The air-polymerized sample was prepared, from monomer purified by method (*b*), in an open flask at 50° with benzoyl peroxide.

In each case polymer was isolated by precipitation in methanol and purified by reprecipitation from acetone solution. The resulting powder was dried in a vacuum at room temperature.

*Degradation Experiments.*—These were carried out in the dynamic molecular still described by Grassie and Melville.[4]

*Infrared Measurements.*—These were made on a Perkin-Elmer Model 13 double-beam spectrophotometer with sodium chloride prism. Monomers were examined in a 0·05-mm. sodium chloride cell, and polymers by the standard potassium chloride disc technique (7 mg./300 mg. of KCl).

The authors thank Dr. G. Eglinton for advice on the interpretation of infrared spectra. Thanks are also due to the D.S.I.R. for the award of a Maintainance Grant (to I. C. M.).

THE UNIVERSITY, GLASGOW, W.2. [*Received, May 15th*, 1956.]

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## 765. *Acylation and Allied Reactions catalysed by Strong Acids. Part XV.* Some Reactions of Simple Alkyl Perchlorates.*

By H. BURTON, D. A. MUNDAY, and P. F. G. PRAILL.

Alkylation of anisole and benzene by methyl, ethyl, *n*-propyl, and the four butyl perchlorates has been studied. Two types of reaction appear to be taking place: (1) nuclear alkylation occurring almost simultaneously with the formation of the alkyl perchlorate in solution, (2) subsequent alkylation by the alkyl perchlorate in certain cases. Detailed mechanisms have not been determined. The possible importance of these types of reaction in the more conventional Friedel–Crafts reactions is discussed.

ALTHOUGH acylation and alkylation by the Friedel–Crafts reaction are considered to be similar, it is also recognised that alkylation processes are more difficult to study because of the numerous side reactions that may occur. In our previous work with acyl and aralkyl perchlorates we have observed that nuclear alkylation and acylation do not seem to be completely analogous and we have made reference to this from time to time.[1] Some further indications of this difference are now presented.

* Part XIV, *J.*, 1955, 3089.

[1] Burton and Praill, (*a*) *J.*, 1951, 522; (*b*) *J.*, 1953, 827.

A preliminary account of the reaction between silver perchlorate and methyl iodide in benzene and in anisole has been reported,[2] and this work has now been extended to incorporate some other simple alkyl compounds. When an alkyl halide is added to a solution of silver perchlorate in an aromatic solvent, metathesis takes place:

$$RX + AgClO_4 \longrightarrow RClO_4 + AgX$$

If the aromatic component is suitably constituted, nuclear alkylation occurs. We found, for example, that methyl, ethyl, *n*-propyl, *n*-butyl, *iso*butyl, *sec.*-butyl, and *tert.*-butyl iodide all gave alkylphenyl methyl ethers when they were added to a solution of silver perchlorate in anisole. Although we were unable to determine the distribution of isomers in the products, it would seem that alkylation occurred predominantly in the *para*-position, since, although the products do not behave as pure substances, we have been unable to isolate any other than *para*-derivatives. However, we do not wish to overemphasize this since prolonged treatment with strong acid in the demethylation of the ethers was a prerequisite to their identification, and it is well known that such conditions might lead to rearrangement of alkyl substituents. With benzene as solvent the *n*-alkyl halides gave extremely small amounts of alkylated derivatives, but, as might be expected, *tert.*-butyl halides gave *tert.*-butylbenzene (0·5 mole per mole of perchlorate) and polyalkyl derivatives, as well as some unsaturated materials. The alkylation of toluene by *tert.*-butyl perchlorate has been reported [3] and it has been stated that *n*-butyl perchlorate does not attack aromatic hydrocarbons in the presence of excess of silver perchlorate.

It will be seen from the Table that for a given time the yield of alkylated anisole increases in the series, $Bu^t > Bu^s > Bu^n > Pr^n > Et > Me$. Further, although the yield of alkylated product increases with time in the case of $Bu^t$ and $Bu^s$, those for the $Bu^n$ and Me derivatives undergo no increase after 4 hours. The significance of these observations will be referred to below.

Addition of nitromethane in any of the above experiments led to the formation of high-boiling intractable materials and resulted in a decreased yield of the monoalkylated derivatives. In some cases it was found that the products contained nitrogen and thus some attack on the solvent must have taken place. In our work on acylation [4] nitromethane was found to be a very suitable polar medium and little or no attack on the solvent was observed, a marked contrast to our present experience. In general, the use of nitromethane was avoided as far as possible.

The alkyl perchlorates are violent explosives,[5,6] so we carried out our experiments under the mildest conditions and did not heat any of the mixtures. Further, it was found necessary to take special precautions in working up the reaction mixtures. We found it extremely difficult to remove all traces of organic perchlorate by the usual washing techniques. This was especially true if the benzene used contained traces of sulphur compounds; in such cases a black amorphous solid separated during the distillation of the product. This undesirable material, which was found to be explosive, could be avoided if the benzene was previously refluxed with Raney nickel. However, we found that the safest procedure was to wash the reaction mixture free from water-soluble perchlorate and then to treat the organic phase with an excess of alcoholic potassium hydroxide. The precipitated potassium perchlorate could then be readily removed. The amount of potassium salt obtained in this way can be taken as a rough measure of unchanged alkyl perchlorate but we do not wish to overestimate the importance of this because the relative rates of hydrolysis of the alkyl perchlorates during the initial washing with water, were not determined.

Whilst our present results are not sufficiently conclusive to attribute them to any particular mechanism it is of interest to see how well they can be explained by available information.

The reaction between alkyl halides and silver salts in hydroxylic solvents has been

[2] Burton and Praill, *Chem. and Ind.*, 1951, 939.
[3] Cauquil, Barrera, and Barrera, *Bull. Soc. chim. France*, 1953, 1111.
[4] Burton and Praill, *J.*, 1950, 2034; 1951, 529.
[5] Meyer and Spormann, *Z. anorg. Chem.*, 1936, **228**, 341.
[6] Burton and Praill, *Analyst*, 1955, **80**, 4.

studied extensively [7-11] and the overall reactions may be represented by the following two simultaneous processes :

$$RX + AgY + R'OH \longrightarrow AgX + HY + ROR' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$RX + AgY \longrightarrow AgX + RY \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where R = alkyl, R' = H or alkyl, X = halide, Y = $NO_3^-$, $OAc^-$, etc. It has been shown that the substitution process is autocatalytic with respect to the silver halide formed and that the heterogeneous reaction is very similar to a homogeneous unimolecular hydrolysis ($S_N1$). Our results with the *n*-alkyl halides indicate that a similar process may be occurring here. The fact that the yield of *n*-butylanisole does not increase with time can be explained in this way. The only other reasonable explanation would be that a state of equilibrium had been reached, thus :

$$BuClO_4 + PhOMe \rightleftharpoons C_4H_4Bu\text{-}OMe + HClO_4$$

That this is unlikely is shown by an experiment in which a pre-formed solution of *n*-butyl perchlorate in nitromethane was found not to have alkylating properties towards anisole under the conditions employed. Now it has been shown that addition of nitromethane, or benzene, to reaction mixtures resulted in a marked decrease in the yield of alkylated product, yet if an equilibrium such as the above was involved we should have expected to detect the formation of some butylanisole. We wish to emphasise the point about the conditions under which these experiments were carried out because alkylation might be brought about under more drastic conditions but we have not yet examined this possibility, owing to the hazardous nature of the experiments.

Our results are probably best explained in terms of reactions (1) and (2) with the aromatic component in place of the hydroxylic compound. Whether the alkylation follows an $S_N1$ or an $S_N2$ mechanism cannot be determined from our present information. Lack of rearrangement of the *n*-alkyl group is no criterion, since nuclear alkylation may be faster than the rearrangement. This is not unlikely, for *n*-alkyl carbonium ions would be much more reactive than tertiary alkyl cations, and reactions where the latter occur are known to be fast. On the other hand, proof of an $S_N1$ mechanism in hydroxylic solvents does not mean that the same mechanism holds for aromatic solvents.

Reactions of the type (1) and (2) undoubtedly hold for secondary and tertiary derivatives also. However, we found that in the case of *sec.*-butyl the yield of butylanisole increased with time; further, a pre-formed solution of *sec.*-butyl perchlorate alkylated anisole in good yield, a reaction analogous to acylation with acyl perchlorates in the absence of silver salts. The yield of *tert.*-butylanisole also increased with time, indicating that *tert.*-butyl perchlorate has some stability in anisole. However, in the presence of nitromethane *tert.*-butyl perchlorate underwent preferential self-condensation with the formation of unsaturated derivatives, behaviour which has also been observed for some allyl [12] and benzyl [1, 13] perchlorates. It has not been possible, therefore, to pre-form a solution of *tert.*-butyl perchlorate. Evidence that *tert.*-butyl perchlorate is itself an alkylating agent is quite clear from the formation of polyalkylbenzenes in our experiments with benzene. *tert.*-Butylbenzene would be expected to be alkylated more readily than benzene in spite of the lower concentration of the former. Again, it has been shown [14] that phenol may be converted in good yield into *p*-*tert.*-butylphenol and 2 : 4-di-*tert.*-butylphenol by mixtures of aqueous perchloric acid and *tert.*-butyl alcohol. The occurrence of carbonium ions in the reactions of some alkyl perchlorates is shown by our results with *iso*butyl perchlorate which gave some tertiary butyl derivatives. It has been reported [15] that optically active 2-bromopentane is nearly completely racemised when it reacts with silver perchlorate in toluene.

[7] Burke and Donnan, *J.*, 1904, **75**, 555.
[8] *Idem*, *Z. phys. Chem.*, 1909, **69**, 148.
[9] Baker, *J.*, 1934, 987.
[10] Hughes, Ingold, *et al.*, *J.*, 1937, 1236, 1243.
[11] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell & Sons, London, 1953, p. 357.
[12] Burton and Munday, *J.*, 1954, 1456.
[13] Praill, Ph.D. Thesis, London, 1954.
[14] Sears, *J. Org. Chem.*, 1948, **13**, 120.
[15] Work by Ingold, Hughes, and Berger, quoted in ref. 3.

Our results indicate that the degree of alkylation which results from the reaction of alkyl halides with silver perchlorate in solution is a function both of the electrophilic activity of the alkyl group and of the nucleophilic activity of the solvent. However, in the absence of more detailed information it would be unjustified to attempt an explanation for the obvious variation in yields in the series Me, Et, $Pr^n$, $Bu^n$. The initial reaction doubtlessly occurs between the alkyl halide and the solvent–$AgClO_4$ complex, with a transition state involving a certain proportion of energised molecules which may be sufficiently active to overcome the energy barrier involved in nuclear alkylation. This is a reaction in which adsorption to the silver halide probably plays an essential part (cf. Dostrovsky and Hughes [16]). We suggest that similar reactions may also play a rôle in other Friedel–Crafts alkylations, as, for example, attack of an alkyl halide on a solvent–metal halide complex. If this be so, the nature of the ternary systems, alkyl halide–aromatic component–metal halide, becomes of increasing importance and interest. The work of Brown and his co-workers [17] shows that some Friedel–Crafts alkylations exhibit a kinetic dependence of first order in each of the three reactants. The reaction we are suggesting would also conform to this, as does the probable simultaneous reaction of the alkyl halide–metal halide complex with the solvent.

Our results show that the ternary reaction may be accompanied by, and then superseded by, a slower reaction of the alkyl perchlorate with the solvent. The latter reaction might follow an $S_N1$ or an $S_N2$ mechanism. These results are summarised by the following equations:

$$C_6H_5R + AgClO_4 \rightleftharpoons C_6H_5R \ldots Ag^{\delta+}ClO_4^{\delta-}$$

$$R'X + C_6H_5R \ldots AgClO_4 \begin{cases} \longrightarrow C_6H_5R + R'ClO_4 + AgX \\ \longrightarrow C_6H_4RR' + HClO_4 + AgX \end{cases}$$

$$C_6H_5R + R'ClO_4 \longrightarrow C_6H_4RR' + HClO_4$$

## Experimental

*Materials.*—Silver perchlorate was treated as described previously.[18] Nitromethane and anisole were dried ($CaCl_2$) and redistilled. Methyl, ethyl, *n*-propyl, and *tert.*-butyl iodide and *tert.*-butyl chloride were redistilled laboratory reagents. *n*-Butyl, *sec.*-butyl, and *iso*butyl iodide were prepared from the corresponding alcohols which were carefully fractionated through a 100-cm. Fenske column with a variable take-off. Benzene was an "AnalaR" reagent which was treated with Raney nickel, dried (Na), and redistilled.

### *Experiments with anisole.*

The alkyl halide (0·05 mole) was either added from a dropping funnel or distilled by using a vacuum-manifold technique, into a cold (<10°) solution of silver perchlorate (0·05 mole) in anisole (0·25 mole). The mixture was stirred by a magnet during the addition. The temperature of the mixture rose slowly to that of the room (20—22°) and was left for the time stated in the Table. Silver halide was filtered off on a weighed, sintered-glass crucible and was washed with ether and with water; the filtrate dropped directly into cold water (250—300 ml.). The ethereal solution was separated and washed with water. A concentrated alcoholic solution of potassium hydroxide (4 g.) was added to the ethereal solution and sufficient ethanol was added to ensure homogeneity. After several hours, any potassium perchlorate which had separated was filtered off and washed with ethanol and aqueous ethanol. The filtrate was diluted with 2—3 vol. of water and extracted thrice with ether. After the combined extracts had been washed with water, the dried ($Na_2SO_4$) solution was evaporated. The residue was then fractionally distilled. In all cases recovery of silver halide was 95—100%.

*Reaction with Methyl Perchlorate.*—The yield of the methyl tolyl ether was not high enough

[16] Dostrovsky and Hughes, *J.*, 1946, 169.
[17] Brown and Grayson, *J. Amer. Chem. Soc.*, 1953, **75**, 6285; cf. papers immediately preceding this; Brown and Jungk, *ibid.*, 1955, **77**, 5584.
[18] Burton and Praill, *J.*, 1950, 2034.

for isolation as such, so the bulk of the unchanged anisole was distilled carefully until the temperature began to rise above 151°. The residue (about 4 g.) was oxidised with alkaline potassium

### *Results*

(All quantities are in moles, unless stated otherwise, and to simplify comparison all experimental values have been corrected to correspond to 0·05 mole of alkyl halide.)

| Expt. no. | Alkyl halide | Reaction time (hr.) | Yield of monosubstn. product | Amt. of $KClO_4$ obtained | Expt. no. | Alkyl halide | Reaction time (hr.) | Yield of monosubstn. product | Amt. of $KClO_4$ obtained |
|---|---|---|---|---|---|---|---|---|---|
| 1 | MeI | 4 | 0·001 | — | 9 | Bu$^n$I | 3½ | 0·015 | 0·023 |
| 2 | ,, | 18 | 0·001 | 0·036 | 10 | ,, | 18½ | 0·030 | — |
| 3 | EtI | 21 | 0·006 | 0·033 | 11 | ,, † | 22 | 0·017 | — |
| 4 | Pr$^n$I | 18 | 0·008 | 0·030 | 12 | Bu$^i$I | 3 | 0·038 | — |
| 5 | Bu$^n$I | 18 | 0·012 | 0·024 | 13 | Bu$^i$Cl | 0·8 | 0·037 | — |
| 6 | ,, | 4 | 0·013 | 0·025 | 14 | ,, | 16 | 0·042 | — |
| 7 | ,, * | 18 | 0·006 | 0·002 | 15 | ,, † | — | — | — |
| 8 | Bu$^n$I † | 18 | — | 0·012 | 16 | Bu$^t$I | 3 | 0·033 | — |

Nearly all the yields quoted are minimal and correspond to the monoalkyl-anisole fraction; usually small amounts of low-boiling material and residue were also obtained.

* Nitromethane as solvent. † Pre-formed perchlorate.

permanganate. The acid produced was isolated in the usual way and identified as *p*-methoxybenzoic acid (m. p. and mixed m. p.).

*Reaction with Ethyl Perchlorate.*—The fraction, b. p. 160—182° (mostly 180—182°) (0·79 g.), was collected. After demethylation with hydrogen bromide in acetic acid, the phenol was isolated as the 3 : 5-dinitrobenzoate, light brown needles (from methanol), m. p. 131—132° (Vogel [19] gives m. p. 132° for *p*-ethylphenyl 3 : 5-dinitrobenzoate).

*Reaction with* n-*Propyl Perchlorate.*—A low-boiling fraction (0·5 g.), b. p. mainly 175—180°, was not identified. The fraction, b. p. 206—214° (mainly 212°), was demethylated with hydrogen bromide in acetic acid. The resulting phenol was converted into its 3 : 5-dinitrobenzoate, m. p. 113—114°, mixed m. p. with 4-*n*-propylphenyl 3 : 5-dinitrobenzoate, 115—116° (below).

4-n-*Propylphenyl* 3 : 5-*Dinitrobenzoate.*—4-*n*-Propylanisole, obtained by reduction of anethole with sodium and ethanol, was demethylated with hydriodic acid and red phosphorus (Klages [20]). The phenol was converted into the 3 : 5-*dinitrobenzoate* which crystallised from methanol as pale yellow needles, m. p. 118° (Found: C, 58·2; H, 4·3; N, 8·5. $C_{16}H_{14}O_6N_2$ requires C, 58·2; H, 4·2; N, 8·5%).

*Reactions with* n-*Butyl Perchlorate.*—A low-boiling fraction, b. p. 160—200° (0·6—0·7 g.), was not identified. The fraction, b. p. 200—234° (mainly 226—234°)/760 mm., or 116—118°/28 mm., was collected as a colourless oil, $n_D^{21}$ 1·5014 (Found: C, 80·5; H, 9·6; Calc. for $C_{11}H_{16}O$: C, 80·5; H, 9·8%). Heilbron and Bunbury [21] give b. p. 120°/19 mm., $n_D^{15}$ 1·5027, for 4-*n*-butylanisole.

Demethylation with hydriodic acid (*d* 1·7) was followed by conversion of the phenol into the aryloxyacetic acid, which crystallised as colourless, fine needles from light petroleum (b. p. 40—60°), m. p. 80—81° (Found: C, 69·5; H, 7·7. Calc. for $C_{12}H_{16}O_3$: C, 69·2; H, 7·7%). Rosenwald *et al.*[22] give m. p. 80—81° for 4-*n*-butylphenoxyacetic acid.

A reaction carried out in nitromethane (52·5 g.) gave a much reduced yield of butylanisole (cf. Table, Expt. 7), but there was more non-distillable residue (1·35 g.).

A solution of *n*-butyl perchlorate in nitromethane (160 g.) was filtered from precipitated silver halide, by use of our alternative technique.[18] Anisole (37 g.) was added, and the mixture left for 18 hr. (cf. Table, Expt. 8). When the mixture was worked up as before it gave no fraction corresponding to butylanisole and only 1·0 g. of high-boiling residue.

*Reaction with* iso*Butyl Perchlorate.*—The fraction, b. p. 90—105° (mainly 102—104°)/25 mm., was redistilled at ordinary pressure, having b. p. 215—220° (mainly 216—219°), $n_D^{19\cdot5}$ 1·5040 (Found: C, 80·4; H, 9·5%). Demethylation with hydriodic acid gave a phenol which solidified; crystallisation of this from light petroleum (b. p. 40—60°) gave colourless needles which, although obviously impure, did not melt completely below 95°. The m. p. of 4-*tert.*-butylphenol was not depressed on admixture with this material.

[19] Vogel, "Practical Organic Chemistry," Longmans Green & Co., London, 1948, p. 657.
[20] Klages, *Ber.*, 1899, **32**, 1438.
[21] Heilbron and Bunbury, "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1946, p. 367.
[22] Rosenwald, Hoatson, and Chenicek, *Ind. Eng. Chem.*, 1950, **42**, 162.

*Reactions with* sec.-*Butyl Perchlorate.*—Some material (0·4 g.), b. p. 180—200°, was obtained, but it still contained some anisole after repeated distillation. Demethylation gave phenol from which the only aryloxyacetic acid that could be obtained was phenoxyacetic acid, colourless flakes [from light petroleum (b. p. 60—80°)] or prisms (from water), m. p. 97° (Found: C, 62·9; H, 5·2. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%). The m. p. of this acid is variously reported as 96°, 97°, and 98—99° (cf. Beilstein's "Handbuch der Organischen Chemie," Vol. VI, p. 161).

Two further fractions were collected: (*A*) b. p. 200—215° (mainly 212—214°), $n_D^{19}$ 1·5056 (Found: C, 80·8; H, 9·8%); (*B*) b. p. 215—220° (mainly 216—218°), $n_D^{19}$ 1·5044 (Found: C, 80·7; H, 10·0%). Heilbron and Bunbury[21] give b. p. 106—108°/16 mm., $n_D^{20}$ 1·5062, for 4-*sec.*-butylanisole.

Demethylation of the above materials gave oily or waxy products from which the solid phenol, m. p. 54—55°, was obtained as colourless needles. Heilbron and Bunbury[21] give m. p. 53—54° for 4-*sec.*-butylphenol.

Attempts to obtain pure aryloxyacetic acids from the demethylated materials were unsuccessful. Some evidence for the presence of 2-*sec.*-butylphenoxyacetic acid was obtained by separating a small amount of crystalline material, m. p. 110—111° (Found: C, 69·0; H, 7·7. Calc. for $C_{12}H_{16}O_3$: C, 69·2; H, 7·7%). Rosenwald *et al.*[22] give m. p. 111° for 2-*sec.*-butylphenoxyacetic acid and 61·5—62·5° for the 4-derivative.

*Reactions with* tert.-*Butyl-Perchlorate.*—The fraction, b. p. 100—110°/22—23 mm. or 210—220°/760 mm., was collected as a colourless, sweet-smelling oil, $n_D^{17\cdot5}$ 1·5050 (Found: C, 80·7; H, 9·7%). Heilbron and Bunbury[21] give b. p. 215—216° for 4-*tert.*-butylanisole.

Demethylation with hydriodic acid gave a solid phenol that crystallised from light petroleum (b. p. 40—60°) as colourless needles, m. p. 98—98·5° (Found: C, 80·1; H, 9·4. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·3%). The m. p. was not depressed by admixture with 4-*tert.*-butylphenol.

When anisole was added to a pre-formed solution of "*tert.*-butyl perchlorate" in nitromethane, no *tert.*-butylanisole was obtained. The nitromethane fraction showed some evidence of unsaturation. There was an intractable high-boiling residue (2·6 g.).

A solution of "*tert.*-butyl perchlorate" was prepared on the vacuum line; no evidence for the formation of free *iso*butene was obtained. When the mixture was worked up in the usual way, a small amount of a yellow unsaturated oil (0·6 g.), b. p. 96—150°/2—3 mm., was obtained. The non-distillable residue (2·3 g.) was a dark brown tar which contained a little nitrogen (Lassaigne).

*Reactions with benzene.*

*Reaction with Methyl Perchlorate.*—Methyl iodide (0·05 mole) was added dropwise to silver perchlorate (0·05 mole) in benzene (0·2 mole) and nitromethane (50·0 g.) at room temperature (*ca.* 20°). The initial separation of silver iodide was fairly rapid and appeared to cease after about 2 hr. The mixture was kept at room temperature for 20 hr. before being worked up in the usual way. The silver halide that had separated was 96% of the theoretical amount.* The dried ($Na_2SO_4$) ethereal extracts were fractionated through a 30-cm. Fenske column. Distillation was discontinued when the temperature at the top of the column had reached 75°, because the residue was then becoming very dark. The residue was diluted with water (50 ml.) and then oxidised by the addition of solid potassium permanganate (15 g.) to the boiling mixture. A few drops of ethyl alcohol were added to remove the last traces of permanganate. The mixture was filtered, and the filtrate concentrated to small bulk; acidification with sulphuric acid caused the separation of solid which was largely inorganic. The mixture was extracted thrice with ether and the ethereal solution was evaporated. Sublimation of the residue gave a few mg. of benzoic acid (m. p. and mixed m. p.).

When the reaction was carried out in benzene alone (230 g.) there was no indication of the formation of benzoic acid.

*Reaction with* n-*Butyl Perchlorate.*—A similar reaction in benzene and with *n*-butyl iodide gave very little evidence for the formation of butylbenzene.

*Reaction with* sec.-*Butyl Perchlorate.*—Here again, there was little evidence of nuclear alkylation in benzene solutions which were left for 5½ or 20 hr. Small quantities (0·6 g.) of orange oil with a b. p. higher than that of benzene were obtained. Attempts to oxidise these materials to identifiable ketonic products with chromic acid were not successful but evidence for the formation of traces of benzoic acid was obtained.

* Under similar conditions, but with methyl cyanide in place of nitromethane, little or no separation of silver halide occurred after 24 hours.

*Reaction with* iso*Butyl Perchlorate.*—After 17 hr., a reaction between freshly distilled *iso*butyl iodide (b. p. 118—120°/769 mm.) (0·1 mole) and an equivalent amount of silver perchlorate yielded material, b. p. 100—180° (mainly 150—180°/760 mm. (5·7 g.), and a fraction, b. p. 75—120°/20 mm. (3·4 g.). The residue (0·3 g.) was a brown oil.

Redistillation of the first fraction gave 3·5 g. of a colourless oil, b. p. 163—170° (mainly 167°). On nitration by the method of Biekart *et al.*[23], 2 : 4-dinitro-*tert.*-butylbenzene was obtained (m. p. and mixed m. p. 58—60°).

Redistillation of the second fraction gave a considerable amount of material, b. p. 170—228°, and a smaller fraction (1·0 g.), b. p. 228—236°. The latter partially crystallised and eventually gave 81 mg. of crystalline material, m. p. 76°, identical with the solid obtained from similar experiments with *tert.*-butyl perchlorate.

*Reaction with* tert.*-Butyl Perchlorate.*—With use of silver perchlorate (0·05 mole) and an equivalent amount of *tert.*-butyl chloride, the reaction was carried out in benzene (230 g.) at room temperature for 30 min. After the benzene was filtered into ice-water it was separated and washed with water, then, without drying, it was evaporated in a vacuum (water-pump) at > 40° (bath). When the solution had been reduced to about 60 ml., alcoholic potassium hydroxide (4 g.) was added. Only a little potassium perchlorate was precipitated and this was filtered off. The filtrate was diluted with water and worked up as before.

Distillation of the product gave a fraction, b. p. 68—70°/28 mm., or 160—164°/760 mm. (3·1 g.), a colourless oil, $n_D^{21}$ 1·4830 (*tert.*-butylbenzene has $n_D^{21}$ 1·4920). The product contained some unsaturated material which could not be removed by distillation. This was probably tri*iso*butene, b. p. 174—176°, $n_D^{21\cdot5}$ 1·4300.

The residue (1·2—1·3 g.) from different experiments frequently solidified to give some crystalline material, colourless prisms (from ether), m. p. 76°; *p*-di-*tert.*-butylbenzene [24] has m. p. 76°.

Nitration of the *tert.*-butylbenzene fraction by the method of Biekart *et al.*[23] gave 2 : 4-dinitro-*tert.*-butylbenzene, colourless prisms (from ethanol), m. p. and mixed m. p. 60—61°.

When the reaction was carried out with benzene (0·2 mole) in nitromethane (60·6 g.) the yield of *tert.*-butylbenzene was only 0·003 mole. Some material (0·6 g.), b. p. 95—100°/9 mm., crystallised to colourless needles, m. p. 73—75°. The viscous orange residue weighed 2·1 g.

We thank Imperial Chemical Industries Limited for a grant toward the cost of this investigation.

QUEEN ELIZABETH COLLEGE (UNIVERSITY OF LONDON), W.8. [*Received May 16th*, 1956.]

[23] Biekart, Dessens, Verkade, and Wepster, *Rec. Trav. chim.*, 1952, **71**, 321.
[24] Baur, *Ber.*, 1894, **27**, 1608.

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## 766. *The Halogenation of Phenolic Ethers and Anilides. Part XVIII.* A Kinetic Method for the Determination of the* ortho/para-*Ratios for Aromatic Ethers.*

By BRYNMOR JONES and EILEEN N. RICHARDSON.

The proportion of *ortho*- and *para*-isomers formed in the chlorination of a number of aromatic ethers has been determined by a kinetic method.

THE classical methods of determining the proportions of isomers formed in an electrophilic aromatic substitution reaction, such as nitration, involve the examination of such physical properties as freezing point, solubility, or density. Although they have frequently been employed with success, and have been the means whereby much of the knowledge relating to the orientating and the directive effects of substituents has been obtained, they necessitate the isolation and purification of the products and, as a result, they are often laborious and at times uncertain.

The present method of analysis of the amounts of *o*- and *p*-isomers formed in nuclear chlorinations, which depends on the difference in the rates of further substitution of the two isomers, permits a rapid estimation of the proportions without isolation of the separate

* Part XVII, *J.*, 1955, 2772.

isomers or indeed of the mixture. The method, first developed by Brynmor Jones [1] for anilides, has now been applied to a range of aromatic ethers. Its success depends largely on the controlled initial chlorination of the phenyl ether to the mixture of monochloro-derivatives without any dichlorination, for the presence of even a small amount of the highly reactive unsubstituted ether would result in a rapid initial rate of chlorination, and lead to a high and erroneous value for the proportion of the more reactive *ortho*-compound. This is apparent from the rates of chlorination of anisole and its chloro-derivatives. The respective rates at 20° are : anisole *ca.* 800, *o*-chloroanisole 4·44, *p*-chloroanisole 1·23, 2 : 4-dichloroanisole 0·0032. Clearly, the accuracy of the method cannot be affected by the gradual accumulation of the dichloro-compound in the reaction mixture, but, with so great a difference in the reactivity of anisole and its *o*- and *p*-chloro-derivatives, a trace of unsubstituted anisole would lead to an erroneous result. The presence of dichlorinated ether is excluded by the method employed, especially since dichlorination is so much slower. The mixtures are also believed to be free from significant amounts of unchlorinated ether, partly because of the degree of control that is possible in the method of preparing them and partly because of the good agreement found earlier [1] between the *ortho*/*para* ratios obtained by this method and those found by other procedures.

The sensitivity of the method depends on the magnitude of the difference in reactivity of the two isomers—in the case of anisole on the rate constants 4·44 and 1·23. Mixtures of the two isomers will have rates of substitution between these limits, the exact value depending on the composition of the mixture. Such a mixture of *o*- and *p*-isomers, obtained by controlled chlorination of an unsubstituted phenyl ether with 1 mol. of chlorine, may therefore be analysed by determining its rate of further substitution, whereupon the coincidence of its velocity with that of a mixture of known composition is observed.

An assessment of the accuracy of this method of analysis has been made [1] by comparing the values of the *ortho*/*para* ratios obtained with those found by other methods.

The proportions of *o*- and *p*-isomers found for three alkyl ethers, two phenoxy-acids, and four substituted benzyl ethers are given in the annexed Table.

| Ether | *ortho*/*para* Proportion | Ether | *ortho*/*para* Proportion |
|---|---|---|---|
| Anisole | 21 : 79 | *p*-Ethylbenzyl phenyl ether | 27 : 73 |
| Phenetole | 20 : 80 | *p*-*tert.*-Butylbenzyl phenyl ether | 27 : 73 |
| Phenyl *iso*propyl ether | 21 : 79 | *p*-Chlorobenzyl phenyl ether | 28 : 72 |
| Phenoxyacetic acid | 16 : 84 | *p*-Nitrobenzyl phenyl ether | 28 : 72 |
| α-Phenoxypropionic acid | 17 : 83 | | |

For these ethers, which fall into three groups, the *ortho*/*para* ratios are essentially the same within any one group. Changes in constitution, such, for example, as anisole to phenyl *iso*propyl ether, and from *p*-ethylbenzyl phenyl ether to *p*-nitrobenzyl phenyl ether do not change the ratio, although they are accompanied by substantial variations in the rates of reaction.

## Experimental

Acetic acid was purified by distillation as described in Part XVII. The distillate had m. p. 16·4°, corresponding to 99·9% purity. The measurements were carried out in 99% acetic acid stable to chlorine.

*Method of Determination of* ortho/para *Ratios.*—For the initial chlorination of an ether to a mixture of *o*- and *p*-isomers, the following procedure was adopted. To 1 mole of the ether dissolved in purified acetic acid in a 100 ml. flask were added 1 mole of chlorine in the form of dichloroamine-T and the amount of water necessary to dilute the acid to 99%. Hydrochloric acid (1/30 mole) was added to initiate chlorination : it produces a low concentration of chlorine which maintains itself throughout the process and prevents the occurrence of a high local concentration and the possibility of disubstitution. When all the chlorine had reacted, an amount of pure silver acetate equivalent to the hydrochloric acid (+5% excess) was added. It is essential for the success of the method that the hydrochloric acid used in the first stage of the chlorination should be removed from solution before proceeding further. When the silver chloride precipitated had settled, a 25 ml. portion of the solution was withdrawn from the flask

[1] Brynmor Jones, *J.*, 1936, 1231.

and the velocity of further substitution was determined in the same way as were the rates of chlorination of mixtures of known composition of the two isomers. The alternative of filtering off the silver chloride was rejected, because of the hygroscopic nature of the medium.

At concentrations greater than 1/30-molar, silver chloride has a catalytic effect on the reaction, but control experiments showed that the presence of this low concentration of silver chloride during reaction of any of these ethers had no effect on the rate constant.

The rates of chlorination of the mixtures were determined by the standard methods used in this series of investigations. The proportions of isomers in the "unknown" mixture were obtained by comparing titres at identical times and not by a comparison of velocity coefficients. Since the mixture consists of two isomers of different reactivity, velocity coefficients obtained from the usual expression for a bimolecular reaction decrease gradually as the reaction progresses.

As an example of the method, the titrations relating to *p*-nitrobenzyl phenyl ether are tabulated. The titres for the "unknown" mixture are seen to fall between those for the mixture containing 27% and those for the mixture containing 30% of *ortho*-isomer, giving a result of 28% of *ortho*-chloro-derivative in the product of chlorination of *p*-nitrobenzyl phenyl ether.

| "Unknown" mixture | | Artificially prepared mixtures | | | |
|---|---|---|---|---|---|
| *ortho* (%) | — | 20 | 23 | 27 | 30 |
| Time (min.) | Titre (ml.) | Titre (ml.) | Titre (ml.) | Titre (ml.) | Titre (ml.) |
| 0 | 7·25 | 7·25 | 7·25 | 7·25 | 7·25 |
| 120 | 5·70 | 5·82 | 5·77 | 5·71 | 5·68 |
| 130 | 5·58 | 5·67 | 5·61 | 5·59 | 5·56 |
| 140 | 5·48 | 5·59 | 5·56 | 5·49 | 5·46 |

*Materials.*—The ethers were prepared by standard methods, particular care being taken to ensure freedom from impurities.

Solids were recrystallised until the rate of chlorination remained unchanged on further purification, and liquids were fractionally distilled under reduced pressure several times.

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## 767. *Bisquaternary Ammonium Salts. Part II.* Salts of 4 : 4′-Diaminostilbene-2 : 2′-disulphonic Acid.†*

By W. G. LEEDS and R. SLACK.

4 : 4′-Diaminostilbene-2 : 2′-disulphonic acid forms sparingly water-soluble, highly crystalline salts with a wide variety of bisquaternary ammonium bases. These salts provide convenient intermediates for the conversion of one soluble salt into another since they are quantitatively decomposed by treatment with appropriate mineral or organic acids.

SEVERAL methods are available for the conversion of a water-soluble salt $B^+X^-$ into a salt $B^+Y^-$ of comparable or greater solubility, but where the base concerned is a bisquaternary ammonium derivative many of the procedures are difficult or inapplicable and an alternative method involving insoluble salts of 2 : 2′-dihydroxy-1 : 1′-dinaphthylmethane-3 : 3′-dicarboxylic acid has recently been described.[1]

This acid exhibits a high degree of specificity in salt formation and for the development of maximum insolubility the cationic component must possess, amongst other things, a minimum chain-length of 8—9 Å. In contrast, it has been found that 4 : 4′-diaminostilbene-2 : 2′-disulphonic acid forms sparingly soluble salts (stoicheiometry 1 : 1) with a

* The paper by Libman, Pain, and Slack, *J.*, 1952, 2305, should be regarded as Part I of this series.
† Some of this work is described in B.P. 748,224.
[1] Barber and Gaimster, *J. Appl. Chem.*, 1952, **2**, 565.

wide variety of bisquaternary ammonium bases and can be used with advantage for the isolation and purification of many such compounds. Thus, although the dicarboxylic acid salts of tetramethylene-1 : 4-bis- and 4-ethylbenzene-1 : ω-bis-trialkylammonium hydroxides are either too soluble or too ill-defined to permit isolation, the corresponding stilbenedisulphonates are relatively insoluble and crystallise well. Most salts of the new series have solubilities between 0·1 and 0·5% in water at 20°. Again, certain mono-acid bases, and diacid bases which contain only one strongly basic group, form similar highly crystalline salts (stoicheiometry 2 : 1); examples of these are given in the Table. All the disulphonates described (see Table) have been prepared by treating an aqueous solution

**4 : 4′-*Diaminostilbene*-2 : 2′-*disulphonates of various quaternary ammonium bases.***

| Cation | Formula | Water content (mol.) | Found (%), followed by Required (%) † C | H | N | S |
|---|---|---|---|---|---|---|
| Hexamethylene-1 : 6-bistrimethylammonium | $C_{26}H_{42}O_6N_4S_2$ | — | 54·2 | 7·6 | 9·3 | 11·3 |
| | | | 54·7 | 7·4 | 9·8 | 11·2 |
| Hexamethylene-1 : 6-bis-1′-methylpyrrolidinium [a] | $C_{30}H_{46}O_6N_4S_2$ | — | — | — | 9·0 | 10·4 |
| | | | | | 9·0 | 10·3 |
| Pentamethylene-1 : 5-bis-1′-methylpyrrolidinium [a] | $C_{29}H_{44}O_6N_4S_2$ | 3·50 | 51·8 | 7·8 | 8·2 | — |
| | | | 51·9 | 7·6 | 8·4 | — |
| | | 5·00 * | 50·0 | 7·5 | 7·9 | — |
| | | | 49·9 | 7·7 | 8·0 | — |
| 4-Ethylbenzene-1 : ω-bistrimethylammonium [b] | $C_{28}H_{38}O_6N_4S_2$ | 4·00 | 50·9 | 7·3 | 8·4 | — |
| | | | 50·8 | 7·0 | 8·5 | — |
| | | 5·00 * | 49·5 | 6·9 | 8·5 | — |
| | | | 49·4 | 7·1 | 8·2 | — |
| 4-Pentylbenzene-1 : ω-bisdimethylethylammonium [b] | $C_{32}H_{48}O_6N_4S_2$ | 1·20 | 58·0 | 7·6 | — | 9·6 |
| | | | 58·1 | 7·4 | — | 9·4 |
| 4-Pentylbenzene-1 : ω-bisdiethylmethylammonium [b] | $C_{32}H_{52}O_6N_4S_2$ | 0·31 | 60·8 | 7·8 | 7·9 | — |
| | | | 60·6 | 7·6 | 8·1 | — |
| 4-Ethyl*cyclo*hexane-1 : ω-bistrimethylammonium (α-form) [b] | $C_{28}H_{44}O_6N_4S_2$ | 4·86 | 49·3 | 8·0 | — | — |
| | | | 49·2 | 7·9 | — | — |
| | | 5·04 * | 48·7 | 7·6 | 8·5 | — |
| | | | 48·9 | 7·9 | 8·2 | — |
| 4-Ethyl*cyclo*hexane-1 : ω-bistrimethylammonium (β-form) [b] | $C_{28}H_{44}O_6N_4S_2$ | 3·64 | 50·7 | 7·9 | 8·2 | — |
| | | | 50·8 | 7·8 | 8·5 | — |
| Tetramethylene-1 : 4-bisdiethylmethylammonium [c] | $C_{28}H_{46}O_6N_4S_2$ | — | — | — | 9·2 | 10·5 |
| | | | | | 9·4 | 10·7 |
| 2 : 4-Dichlorophenoxymethyldimethyloctylammonium [d] | $C_{45}H_{66}O_8N_4Cl_4S_2$ | 0·64 | 55·7 | 6·7 | 5·4 | — |
| | | | 55·1 | 6·6 | 5·4 | — |
| ω-*p*-Aminophenoxyhexyltrimethylammonium | $C_{44}H_{68}O_8N_6S_2$ | 3·42 | 57·2 | 8·1 | 9·1 | — |
| | | | 56·8 | 7·8 | 9·0 | — |
| 4-Hexyloxybenzene-1 : ω-bistriethylammonium [e] | $C_{38}H_{58}O_7N_4S_2$ | 2·54 | 57·7 | 8·0 | 7·2 | — |
| | | | 57·6 | 8·0 | 7·1 | — |

* Alternative values for different samples exhibiting varying degrees of hydration. † Calculated values for hydrated material where necessary.

[a] Di-iodide described by Libman, Pain, and Slack.[2] [b] Ashley and Leeds.[3] [c] Prepared by K. Gaimster (see Barber and Gaimster [1] for other salts). [d] Chloride described by Barber and Green.[4] [e] Atkinson, Heywood, and Leeds.[5]

of a soluble quaternary salt with the appropriate amount of disodium or diammonium 4 : 4′-diaminostilbene-2 : 2′-disulphonate in water. The high solubility of the sodium and ammonium salts precludes inorganic contamination of the products. The salts are easily recrystallised from water and some of them separate with varying amounts of water of crystallisation. Vacuum-drying at 100° gives the anhydrous salt which are hygroscopic. The stilbenedisulphonates, the solubilities of which increase greatly with increasing temperature, can be converted into soluble quaternary salts by dissolution or suspension in water and precipitation of the insoluble 4 : 4′-diaminostilbene-2 : 2′-disulphonic acid by addition of the calculated amount of acid corresponding to the desired anion, preferably

[2] Libman, Pain, and Slack, *J.*, 1952, 2305.
[3] Ashley and Leeds, unpublished work.
[4] Barber and Green, *J. Appl. Chem.*, 1954, **4**, 115.
[5] Atkinson, Heywood, and Leeds, unpublished work.

below 60°. Quantitative decomposition occurs even with relatively weak acids such as tartaric.

4 : 4′-Diaminostilbene-2 : 2′-disulphonic acid is readily available commercially and has been used for many years in the dyestuffs industry. For the present purpose, however, the use of pure acid is important since crude commercial samples—particularly those which give deep red solutions in aqueous ammonia—often yield highly coloured derivatives. Occasional slight discoloration (presumably photo-instability) of diamino-disulphonates prepared from the pure acid has also been observed but this does not lead to difficulties during subsequent decompositions nor does it appear to affect analytical figures. Pure reagent can easily be obtained by acid decomposition of a *recrystallised* sample of a suitable quaternary ammonium salt, *e.g.*, hexamethylene-1 : 6-bis(trimethylammonium) 4 : 4′-diaminostilbene-2 : 2′-disulphonate.

## Experimental

Examples given in detail illustrate general techniques. Other 4 : 4′-diaminostilbene-2 : 2′-disulphonates are prepared similarly.

*Hexamethylene-1 : 6-bistrimethylammonium 4 : 4′-Diaminostilbene-2 : 2′-disulphonate.*—Hexamethylene-1 : 6-bistrimethylammonium bromide (3·62 g.) in water (15 c.c.) was added to a solution of disodium 4 : 4′-diaminostilbene-2 : 2′-disulphonate (4·14 g.) in water (10 c.c.) at 50°. The pale yellow salt (5·34 g.) was collected after 12 hr. at 2° and was recrystallised from water, to give the pure compound (4·7 g.), m. p. 280° (decomp.), which contains water of crystallisation. Prolonged drying at 100° *in vacuo* over phosphoric oxide gave the *anhydrous salt*, m. p. 293—294° (decomp.). The solubility of the salt in water at 12° is approx. 0·4%.

*Hexamethylene-1 : 6-bis-1′-methylpyrroldinium 4 : 4′-diaminostilbene-2 : 2′-disulphonate*, m. p. 285—290° (decomp.), was prepared in a similar manner (solubility at 12° approx. 0·15%).

Hexamethylene-1 : 6-bis(trimethylammonium hydrogen tartrate) was prepared from the 4 : 4′-diaminostilbene-2 : 2′-disulphonate (5·7 g.) in water (15 c.c.) at 35—40° by treatment with (+)-tartaric acid (3·0 g.) in water (10 c.c.). The 4 : 4′-diaminostilbene-2 : 2′-disulphonic acid was collected and washed with cold water, and the combined filtrates were evaporated to dryness. The resulting syrup, after being treated with cold alcohol, gave the hydrogen tartrate (4·45 g.), m. p. 180—182° after recrystallisation from methanol (Barber and Gaimster [2] give m. p. 180—185°).

*Pentamethylene-1 : 5-bis-1′-methylpyrrolidinium 4 : 4′-Diaminostilbene-2 : 2′-disulphonate.*—The corresponding dibromide, a highly deliquescent, colourless, crystalline solid (4 g., from pentamethylene dibromide and 1-methylpyrrolidine in methanol), in water (10 c.c.) was added to a warm filtered solution of 4 : 4′-diaminostilbene-2 : 2′-disulphonic acid (4 g.) in water (15 c.c.) and aqueous ammonia (*d* 0·88; 5 c.c.). The pale yellow *salt* (4·6 g.) was collected after 3 hr. at 2°, washed with water, and dried in air. It slowly developed a pale red colour on the crystal surfaces but remained analytically pure, m. p. 305° (decomp.).

4-Ethylbenzene-1 : ω-bistrimethylammonium 4 : 4′-diaminostilbene-2 : 2′-disulphonate, m. p. >230° (decomp.), was prepared similarly from 4-ethylbenzene-1 : ω-bis(trimethylammonium iodide) and was converted into the corresponding dihydrogen phosphate by treating an aqueous suspension [1·812 kg., 2·71 moles of anhydrous salt in water (21 l.)] with phosphoric acid (100% recovery) and was filtered off and washed with water. The combined filtrates were filtered (charcoal) and concentrated under reduced pressure to 2 l. After being filtered (charcoal), the solution was added to methanol (4 l.) and acetone (4 l.), to give the colourless microcrystalline *dihydrogen phosphate tetrahydrate* (1·86 kg., 90%), m. p. 199° (decomp.) (Found: N, 5·8; P, 12·7; $H_2O$, 14·7. $C_{14}H_{30}O_8N_2P_2,4H_2O$ requires N, 5·7; P, 12·7; $H_2O$, 14·7%).

*4-Ethylcyclohexane-1 : ω-bistrimethylammonium 4 : 4′-diaminostilbene-2 : 2′-disulphonate.*—Sodium hydroxide (486 g.) in water (1 l.) was added gradually to a stirred solution of 2-(4-amino*cyclo*hexyl)ethylamine dihydrochloride [3] (α-form) (323 g.), and dimethyl sulphate (1·31 kg.) was added dropwise at 50° during 45 min. (external cooling). After a further hour at 50°, the filtered solution was added to 4 : 4′-diaminostilbene-2 : 2′-disulphonic acid (635 g.) in water (3·2 l.) and ammonia (*d* 0·88; 550 c.c.). The highly crystalline, pinkish-yellow 4 : 4′-diaminostilbene-2 : 2′-disulphonate (973 g.) separated immediately. Dehydration at 50° gave a primrose-yellow product which reverted to a stable hydrate, m. p. 290° (decomp.), in moist air.

The corresponding chloride was prepared from the 4 : 4′-diaminostilbene-2 : 2′-disulphonate (1·925 kg.) by treatment in aqueous suspension at 20° with 5·8N-hydrochloric acid (982 c.c.).

Recrystallisation from ethanol–acetone gave the *chloride trihydrate* (770 g., 77%), m. p. 317° (decomp.) (Found: C, 48·0; H, 10·8; N, 7·7; Cl, 20·5; $H_2O$, 15·0. $C_{14}H_{32}N_2Cl_2,3H_2O$ requires C, 47·6; H, 10·8; N, 7·9; Cl, 20·1; $H_2O$, 15·3%).

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## 768. *The Strengths of Arylmethanols as Secondary Bases.*

By V. Gold.

The relative strengths of four unsubstituted arylmethanols as secondary bases are shown to be in agreement with values calculated by simple molecular-orbital theory. The calculations are based on the assumption that π-electron energies make the most important structure-sensitive contribution to the free energy of ionisation and that the π-electron energy of di- and tri-phenylcarbonium ions may be calculated in the same way as if the conjugated systems were perfectly coplanar. It is inferred that in the series benzyl alcohol–diphenylmethanol–triphenylmethanol π-electron energies, and not steric strains, decide the relative strengths of secondary bases.

Arylmethanols have a tendency to ionise in strongly acidic solutions as secondary bases,[1] according to the formal equation:

$$ROH + H^+ \rightleftharpoons R^+ + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (i)$$

The best known example of this equilibrium is the ionisation of triphenylmethanol and its derivatives in sulphuric acid solutions. The concept of the acidity function [1,2] $J_0$ allows the strengths of different secondary bases to be expressed in a quantitative fashion over a considerable range of values in terms of the constant $K_{ROH}$, which governs the equilibrium (i). On this basis, comparative measurements for a number of arylmethanols have recently been reported [3] (though with different symbols). It has been pointed out [4] that there is quantitative disagreement between some of these measurements and the less extensive results of another investigation [5] but, in any case, the data appear to be adequate for the following consideration of the gross structural factors which govern the strengths of unsubstituted arylmethanols as secondary bases.

The standard free-energy change in reaction (i) (and hence the related equilibrium constant $K_{ROH}$) may, in principle, depend on a number of things. Changes in resonance energy and steric compression energy on going from the alcohol to the carbonium ion are likely to be the most important structure-sensitive factors.[6] In view of the bulkiness of the carbonium ions it is probable that changes in the free energy of solvation would play only a minor rôle. An exact analysis of the problem is obviously impossible at present. In their discussions of it Deno *et al.*[6,7] concluded that the release of steric strain on formation of the carbonium ion was the important variable term, and that the change in resonance energy accompanying ionisation was the same for di- and tri-arylmethanols. As no theoretical estimate of any of the factors appears to have been attempted, we have now used a simple molecular-orbital calculation to assess the importance of π-electron energies and to see if a correlation exists between the change in resonance energy and the constant

[1] Gold and Hawes, *J.*, 1951, 2102.
[2] Gold, *Chem. and Ind.*, 1955, 172; *J.*, 1955, 1263.
[3] Deno, Jaruzelski, and Schriesheim, *J. Amer. Chem. Soc.*, 1955, **77**, 3044.
[4] Gold and Satchell, *J.*, 1956, 1635.
[5] Williams and Bevan, *Chem. and Ind.*, 1955, 171.
[6] Cf. Deno, Jaruzelski, and Schriesheim, *J. Org. Chem.*, 1954, **19**, 155.
[7] Deno and Schriesheim, *J. Amer. Chem. Soc.*, 1955, **77**, 3051.

$K_{ROH}$. The method of calculation is analogous to that described for hydrocarbon acids [8] and primary bases [9] and for the ionisation of triphenylmethyl halides.[10]

In calculating the π-electron energies of the carbonium ions it was assumed that the twisting out of coplanarity which is due to the bulk of the phenyl group does not cause the resonance energy to fall greatly below the value applicable to a coplanar system. On this basis, if the changes in the constant $K_{ROH}$ are entirely governed by changes in π-electron energies, we should have :

$$-RT \ln K_{ROH} = (E_\pi)_{R^+} - (E_\pi)_{ROH} + \text{Constant} \quad . \quad . \quad . \quad . \quad \text{(ii)}$$

where $E_\pi$ represents the contribution from the π-electron energies to the enthalpies of the hypothetical planar molecules indicated by the second subscript. The value of $(E_\pi)_{ROH}$ was obtained by considering each of the aryl groups attached to the exocyclic carbon atom to contribute an isolated conjugated system. The results of the calculation for a few typical secondary bases are tabulated.

The results in the column headed $(\Delta E_\pi - \alpha)\beta^{-1}$ are expressed in terms of the characteristic energy parameter β (the resonance integral) of the molecular-orbital theory. It is known empirically that β has a value of about −18 kcal./mole when, as in our case, no correction is applied in the calculation for changes in compressional energy [11] and overlap is neglected.

The calculation may be compared with experiment by plotting the available experimental values of $pK_{ROH}$ against $(\Delta E_\pi - \alpha)$. According to the measurements by Deno, Jaruzelski, and Schriesheim [3] the $pK_{ROH}$ values for triphenylmethanol, diphenylmethanol, and 9-fluorenol are 6·63, 13·3, and 14·0 respectively. From the value for 2 : 4 : 6-trimethylbenzyl alcohol (17·38) and a consideration of the effect of methyl substitution in di- and tri-phenylmethanol it is estimated that the $pK_{ROH}$ value for benzyl alcohol lies in the range 22—27 (see Appendix I). These results are plotted in Fig. 1. A relation, which is linear within the limits of error, is found to exist between $\Delta E_\pi$ and $pK_{ROH}$, the slope of the line leading to the value $\beta = -22 \pm 3$ kcal./mole, *i.e.*, close to the value to be expected if the basic assumption of the calculation—that resonance energy is the dominant structural influence governing the strengths of these secondary bases—is correct. The agreement does not constitute a proof but is taken as circumstantial evidence for the correctness of the assumptions.

| R | $(E_\pi)_{R^+}$ | $(E_\pi)_{ROH}$ | $(\Delta E_\pi - \alpha)\beta^{-1}$ |
|---|---|---|---|
| Ph·$CH_2$ | $7\alpha + 8{\cdot}72\beta$ | $6\alpha + 8{\cdot}00\beta$ | 0·72 |
| $Ph_2CH$ | $13\alpha + 17{\cdot}30\beta$ | $12\alpha + 16{\cdot}00\beta$ | 1·30 |
| $Ph_3C$ | $19\alpha + 25{\cdot}79\beta$ | $18\alpha + 24{\cdot}00\beta$ | 1·79 |
| 1-$C_{10}H_7$·$CH_2$ | $11\alpha + 14{\cdot}49\beta$ | $10\alpha + 13{\cdot}68\beta$ | 0·81 |
| 2-$C_{10}H_7$·$CH_2$ | $11\alpha + 14{\cdot}42\beta$ | $10\alpha + 13{\cdot}68\beta$ | 0·74 |
| 9-Anthrylmethyl | $15\alpha + 20{\cdot}24\beta$ | $14\alpha + 19{\cdot}31\beta$ | 0·93 |
| $(p\text{-}C_6H_4Ph)_3C$ | $37\alpha + 51{\cdot}01\beta$ | $36\alpha + 49{\cdot}15\beta$ | 1·86 |
| $(p\text{-}C_6H_4Ph)_3CPh$ | $31\alpha + 42{\cdot}61\beta$ | $30\alpha + 40{\cdot}77\beta$ | 1·84 |
| 9-Fluorenyl | $13\alpha + 17{\cdot}72\beta$ | $12\alpha + 16{\cdot}38\beta$ | 1·34 |
| $p\text{-}C_6H_4Ph$·$CH_2$ | $13\alpha + 17{\cdot}14\beta$ | $12\alpha + 16{\cdot}38\beta$ | 0·76 |
| $m\text{-}C_6H_4Ph$·$CH_2$ | $13\alpha + 17{\cdot}10\beta$ | $12\alpha + 16{\cdot}38\beta$ | 0·72 |
| 9-Phenyl-9-fluorenyl | $19\alpha + 26{\cdot}22\beta$ | $18\alpha + 24{\cdot}38\beta$ | 1·84 |
| 1-$C_{10}H_7$·$CPh_2$ | $23\alpha + 31{\cdot}54\beta$ | $22\alpha + 29{\cdot}68\beta$ | 1·86 |
| $(m\text{-}C_6H_4Ph)_3C$ | $37\alpha + 50{\cdot}95\beta$ | $36\alpha + 49{\cdot}15\beta$ | 1·80 |

The proximity of the points for diphenylmethanol and 9-fluorenol may be regarded as particularly significant since in the latter case the ion is planar, whereas it need not be so in the former. If the model used by Deno *et al.*[6] (according to which only one ring conjugates with the exocyclic carbon atom in di- and tri-arylcarbonium ions, the other ring or rings being unable to share in the conjugation because of their unfavourable orientation) were correct, this agreement would be out of place.

This simple resonance theory would probably be inapplicable to arylmethanols containing more bulky groups, such as naphthyl and anthryl groups perhaps, and measurements

[8] Wheland, *J. Chem. Phys.*, 1934, **2**, 479.
[9] Gold and Tye, *J.*, 1952, 2184.
[10] Streitwieser, *J. Amer. Chem. Soc.*, 1952, **74**, 5288.
[11] Lennard-Jones, *Proc. Roy. Soc.*, 1937, *A*, **158**, 280; Coulson and Altmann, *Trans. Faraday Soc.*, 1952, **48**, 293.

of the basic strength of the corresponding alcohols may yield quantitative information regarding the π-electron energies of twisted conjugated systems.

In view of the apparent success of this treatment, it remains to inquire whether the experimental data on which the model used by Deno *et al.* was based may have an alternative explanation. The evidence adduced falls into two main groups. First, it was noted that there was an almost constant difference between p$K$ for $Ar_3C{\cdot}OH$ and p$K$ for $Ar_2CH{\cdot}OH$ for a number of substituted phenyl groups Ar. This indicates that two substituent groups in diphenylmethanol exert the same influence on the $pK_{ROH}$ value as three of the same kind in triphenylmethanol. A similar relation was also noted for single substituent groups in di- and tri-phenylmethanol. Secondly, there is a similarity in absorption spectra between several pairs of correspondingly substituted di- and tri-arylcarbonium ions.

The interpretation of the absorption spectra will have to await more detailed knowledge concerning the electron systems of twisted conjugated systems, but the substituent effects may be qualitatively explained also in terms of our model.

Consider the effect of a single electron-attracting group X in the di- and in the triphenylcarbonium ion. The electron-withdrawal of X from the exocyclic carbon atom will

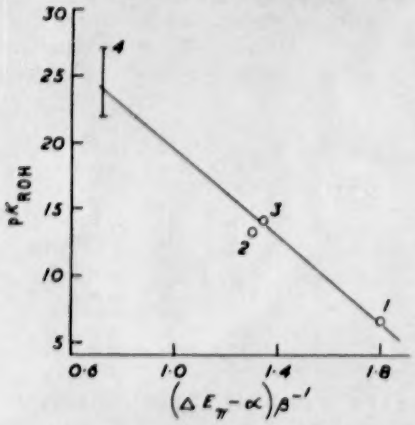



FIG. 1.
1, *Triphenylmethanol.*
2, *Diphenylmethanol.*
3, *9-Fluorenol.*
4, *Benzyl alcohol.*

be partially compensated by electron-release from the unsubstituted phenyl group(s), which, according to the situation, can act as " electron sources " or " sinks." In this way the effect of X is " diluted " by being spread over the other rings and will, in first approximation, be inversely proportional to the total number of rings, as observed by Deno and Schriesheim.[7]

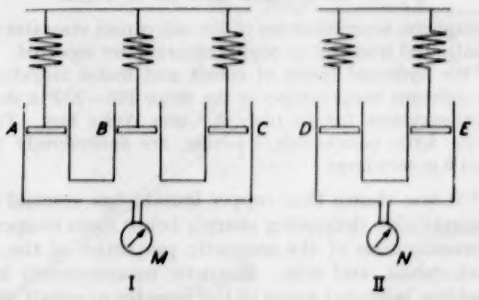
It has also been observed that two identical substituent groups in diphenylmethanol effect the same change in p$K$ for diphenylmethanol as three of the same kind in p$K$ for triphenylmethanol, and the following is suggested as a tentative explanation of this. The inductive effect of a substituent group in a highly polarisable system of many mobile electrons is more appropriately described as a change in electrical potential at a certain carbon atom in the molecule than as the migration of a certain amount of charge from the substituent group to that atom. Thus, the presence of a group X in the ring of the phenylcarbonium ion will cause a change in the electrical potential (or " pressure " of electrons) at the α-carbon atom. It is this potential (and not the net electric charge) which parallels the inductive contribution to the ionisation tendency of the molecule. On going from the mono- to the di-phenylcarbonium ion (and, analogously, to the triphenylcarbonium ion), the potential at the exocyclic carbon atom will be similarly affected by the substituent only if both rings exert the same effect. To a first approximation and for groups of moderate inductive strength, this may be expected to be the case if the rings are identically substituted. When one of the rings remains unsubstituted we have the case of the

" dilution " effect discussed above. How correct or useful this picture of the inductive effect may be in general cannot be judged on the evidence considered so far. To clarify the basic concepts involved, a crude mechanical analogue of the model is described in Appendix II.

### Appendix I. $pK_{ROH}$ *value for benzyl alcohol.*

The approximate estimate (22—27 units) is based on the following three, largely independent, lines of reasoning : (i) If we assume the difference in $pK_{ROH}$ values between diphenylmethanol and benzyl alcohol to be the same [6] as that between dimesitymethanol and 2 : 4 : 6-trimethylbenzyl alcohol, we obtain p$K$ 24·1 for benzyl alcohol. (ii) The effects of *o*- and *p*-methyl substituents on the $pK_{ROH}$ value of diphenylmethanol are known.[3] We now assume that the effect of a *p*-methyl group in benzyl alcohol is the same as that of two *p*-methyl groups in diphenylmethanol, and that the effect of two *o*-methyl groups in benzyl alcohol is twice that exerted by two methyl groups (in the 2 : 2′-positions) in diphenylmethanol. This leads to the value p$K$ 22·0 for benzyl alcohol. A similar consideration of the effect of methyl substituents in triphenylmethanol leads to a higher value (~27). Since triphenylmethanol differs from benzyl alcohol in structure rather more than does diphenylmethanol, the lower value is preferred. (iii) The effectiveness of substituent groups in the ring on dissociation constants of aromatic acids is largely determined by the distance of the acidic group from the aromatic

Fig. 2.




ring and its manner of attachment (see ref. 12, Figs. 36 and 39). On this basis, the methyl groups in 2 : 4 : 6-trimethylbenzyl alcohol might each be expected to have an effect similar in magnitude to that of a *p*-methyl group in aniline. (*o*-Methyl groups in aniline are not comparable because of the peculiar steric inhibition of resonance which arises in this structure. In acids where this *ortho*-effect is absent, as in phenols, the effects of *ortho*- and *para*-substituents are roughly equal.) This procedure leads to p$K$ = 18·8 for benzyl alcohol. However, this value must be too low, as the calculation ignores the hyperconjugative effect of the methyl group. This is likely to be stronger in the phenylcarbonium ion than in the anilinium ion. The difference in the effects on a dissociation constant which a substituent group exerts from the *meta*- and the *para*-position is a measure of the conjugative effect of that group. In aniline this difference amounts to 0·4 unit for the methyl group and 0·5 unit for chlorine, *i.e.*, methyl and chlorine substituents have very similar effects. In triphenylmethanol and in diphenylmethanol the differential effect of chlorine substitution, in all *para*-positions on the one hand and in one *meta*-position in each ring on the other, amounts to 3·3 units,[3] *i.e.*, in these *para*-substituted arylmethanols there appears to be an additional base-strengthening effect of ~2·8 p$K$ units, due to conjugation. If the effect of the methyl group is again about the same as that of chlorine, and if three methyl groups in benzyl alcohol have three times the effect of a chlorine atom in the *para*-position of each ring in diphenylmethanol, the calculated value of p$K$ for benzyl alcohol is ~27.

### Appendix II. *Mechanical analogue of inductive effect in system of mobile electrons.*

The three benzene rings in the triphenylcarbonium ion are compared to three cylinders which are attached to a common manifold (Fig. 2, I). The cylinders are closed by weightless and frictionless pistons, and the system is filled with an ideal gas. The upward motion of the

[13] Branch and Calvin, " The Theory of Organic Chemistry," Prentice-Hall, New York, 1941.

pistons is limited by springs (obeying Hooke's law) under compression. Similar systems with two cylinders (Fig. 2, II) or one cylinder represent the di- and the mono-phenylcarbonium ions respectively. The pressure at *M* and *N* is the analogue of the electrical potential at the exocyclic carbon atom.

The introduction of an electron-repelling substituent group into one of the rings may be likened to placing a *small* weight *w* on one of the pistons (say, *A*). This will cause compression of the gas and of the springs attached to *B* and *C*, a slight release of the compression of the spring attached to *A*, and an increase of the pressure registered by the manometer *M* which is attached to the manifold. If the volume of the manifold is small compared with that of the pistons, the following statements—which correspond to the substituent effects discussed in the last two paragraphs of the paper—follow from Boyle's law and Hooke's law: (1) If a weight *w* is placed on *A*, and an equal weight *w* on *D*, then the pressure changes at *M* and *N* are in the ratio 2 : 3, *i.e.*, they are inversely proportional to the number of cylinders. (2) Three equal weights *w* placed respectively on *A*, *B*, and *C* change the pressure at *M* as much as two of the same weights, placed at *D* and *E* respectively, change the pressure at *N*.

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## 769. *Magnetic Properties of Some Metal Carboxylates.*

By R. C. HERRON and R. C. PINK.

The paramagnetic susceptibilities of the anhydrous stearates and laurates of nickel, cobalt, and iron and of copper stearate are reported. Results are included for the hydrated forms of cobalt and nickel laurates. Measurements at five different temperatures in the range 105—333° K show that only the copper carboxylates fail to obey a Curie–Weiss law. The magnetic moments of the ferric compounds, however, are anomalously low, and the Weiss constant θ is very large.

IN a previous paper [1] it was shown that copper laurate has unusual magnetic properties, the paramagnetic susceptibility decreasing sharply below room temperature. The present paper describes an investigation of the magnetic properties of the anhydrous stearates and laurates of nickel, cobalt, and iron. Magnetic measurements have also been made on copper stearate and the hydrated forms of the laurates of cobalt and nickel.

The metallic soaps have presented various features of interest to chemists for the past thirty years, in particular their behaviour in solution, both aqueous and organic, their polymorphic transitions, and their surface properties. In spite of this, and their economic importance,[2] the structure of these compounds has largely been ignored. The complexity of a single molecule, together with the non-crystallinity of the bulk compounds, has so far impeded complete structural analyses by *X*-ray methods of all but the alkali and alkaline-earth soaps. Also, the aggregation which occurs in common organic solvents [3] greatly reduces the significance of dipole-moment measurements in solution.[4]

### EXPERIMENTAL

*Preparation and Purification of Materials.*—Stearic acid was purified by repeated crystallisation from aqueous ethanol. Lauric acid was similarly purified from "AnalaR" acetone. M. p.s were 69·2° and 43·9° respectively.

All the metal soaps were prepared by metathesis at 40° of the corresponding sodium soaps in aqueous ethanol.[5] The precipitated soaps were washed with distilled water till free from precipitant and then with cold aqueous ethanol to remove free acid, then dried by suction at a water pump and stored over calcium chloride. Prepared in this way nickel laurate and cobalt laurate were both obtained as the dihydrates,[6] which were readily dehydrated by boiling them in organic solvents. Ferric soaps made by precipitation from aqueous solutions have been

[1] Gilmour and Pink, *J.*, 1953, 2198.
[2] "Encyclopædia of Chemical Technology," Interscience Publ. Inc., 1950, Vol. V, p. 203.
[3] Nelson and Pink, *J.*, 1952, 1744.
[4] Gilmour, Nelson, and Pink, *Nature*, 1953, **171**, 1075.
[5] Pink, *J.*, 1938, 1252.
[6] Cf. Oudemans, *J. prakt. Chem.*, 1863, **89**, 206.

described as basic compounds.[7] In these experiments, however, it was found that, provided the ferric soaps were dried without heating (*e.g.*, *in vacuo* over $P_2O_5$) the neutral soaps were obtained. The absence of hydroxyl groups in the products was confirmed by infrared absorption measurements on paraffin mulls (Perkin–Elmer Model 21 spectrometer). Nickel laurate dihydrate also decomposed when heated, losing lauric acid rapidly by volatilisation : a sample heated at 105° for 6 hr. lost 23·6% by weight. Part of the lauric acid volatilised was recovered and identified by a mixed m. p. determination. The water of hydration may be removed by desiccation *in vacuo* ($P_2O_5$ or $H_2SO_4$), the anhydrous soap being rehydrated rapidly in air. By means of a series of desiccation experiments with various strengths of sulphuric acid the dissociation pressure of the hydrate was estimated to be 12 mm. at 16° and 22 mm. at 45°, giving a value of 17·8 kcal. mole$^{-1}$ for the heat of dissociation, comparable with that of crystalline hydrates. Dehydration is accompanied by a slight but distinct colour change from pale green

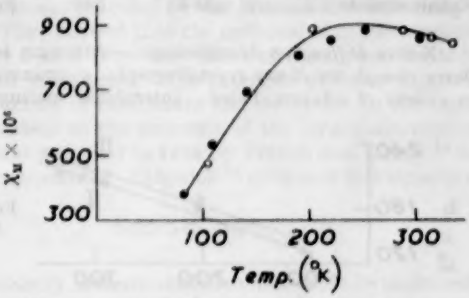



FIG. 1. *Effect of temperature on susceptibility of copper carboxylates*

○ *Cupric stearate.*
● *Cupric acetate monohydrate (plotted from Guha's data [10]).*

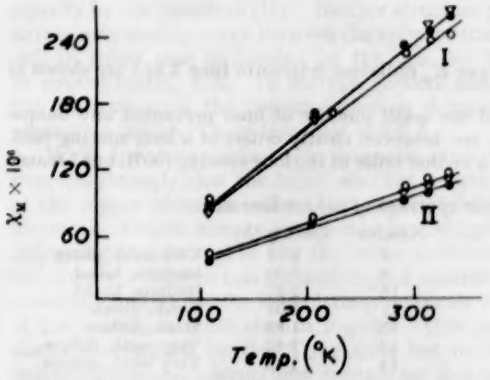



FIG. 2. *Effect of temperature on susceptibility of nickel and cobalt carboxylates.*

(i) *Nickel,* (ii) *cobalt compounds.*

● *Anhydrous laurates.*
○ *Anhydrous stearates.*
▽ *Hydrated laurates.*

to pale yellow. The colour change on hydration is more marked with the cobalt soaps, the dihydrates being rose-pink, the anhydrous compounds purple. Analytical data for the anhydrous compounds are shown in the Table : in all cases the compounds obtained were the neutral soaps.

| | Laurates | | | Stearates | | | |
|---|---|---|---|---|---|---|---|
| | Ni | Co | Fe(ic) | Ni | Co | Fe(ic) | Cu |
| Metal, found (%) . . | 12·8 | 12·65 | 8·5 | 9·1 | 9·6 | 6·4 | 9·9 |
| ,, calc. (%) . . | 12·8 | 12·9 | 8·5 | 9·4 | 9·4 | 6·2 | 10·1 |

*Magnetic Measurements.*—Susceptibility measurements were made by the Gouy method on the finely powdered solids, by means of an apparatus described previously.[8] The solids were packed in the specimen tube at 10—12 mm. Hg. Temperatures were measured with a copper–constantan thermocouple, calibrated at low temperatures according to Scott's method.[9] All the magnetic measurements were made with the specimen tube in an atmosphere of oxygen-free (B.O.C. " white-spot ") nitrogen. The magnetic data are shown in Figs. 1—3 where $\chi_M$ is the

[7] Soyenkoff, *J. Phys. Chem.*, 1930, **34**, 2519.
[8] McDonnell, Pink, and Ubbelohde, *Trans. Faraday Soc.*, 1950, **46**, 156.
[9] Scott, *J. Res. Nat. Bur. Stand.*, 1940, **25**, 459.

value of the molar susceptibility in c.g.s. units corrected for the diamagnetic contribution to the susceptibility from the organic part of the molecule. Standard Pascal corrections were employed throughout. In Fig. 1 the data for hydrated copper acetate obtained by Guha [10] are included for comparison. The effective magnetic moment, $\mu_{eff.}$, and the Weiss constant $\theta$ [derived from the relationship $\chi_M = C/(T - \theta)$ where $C$ and $\theta$ are constants] for the nickel, cobalt, and iron soaps are shown in Table 1.

TABLE 1. *Magnetic constants of metal carboxylates.*

| | $-\theta$ (°K) | $\mu_{eff.}$ (B.M.) | | $-\theta$ (°K) | $\mu_{eff.}$ (B.M.) |
|---|---|---|---|---|---|
| Nickel stearate ..... | 18·1 | 3·35 | Cobalt laurate ..... | 12·7 | 5·06 |
| Nickel laurate ..... | 11·6 | 3·22 | Cobalt laurate dihydrate | 11·2 | 5·07 |
| Nickel laurate dihydrate | 0·0 | 3·18 | Ferric stearate ..... | 377·9 | 5·04 |
| Cobalt stearate ..... | 18·5 | 5·00 | Ferric laurate ..... | 338·1 | 4·98 |

X-*Ray Diffraction Measurements.*—Attempts to produce single crystals of copper laurate, large enough for $X$-ray crystallographic examination, either from the melt or from solution in a variety of solvents, failed. Interplanar spacings obtained from powder photographs taken

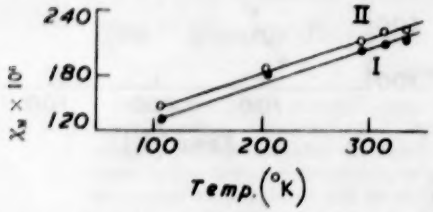



FIG. 3. *Effect of temperature on susceptibility of ferric carboxylates.*
(i) *Ferric laurate*; (ii) *ferric stearate.*

with a 3 cm. radius camera and filtered copper $K_\alpha$ radiation (exposure time 3 hr.) are shown in Table 2.

Both the accuracy of measurement and the small number of lines prevented any unique assignment of indices. The first four lines are, however, clearly orders of a long spacing (003, 004, 005, 006). Line 5 could be indexed as a further order of the long spacing (007), but because

TABLE 2. *Interplanar spacings of copper laurate.*

| Number | Spacing (Å) | | Number | Spacing (Å) | |
|---|---|---|---|---|---|
| 1 | 10·81 | Strong, sharp | 8 | 2·82 | Very weak, sharp |
| 2 | 7·92 | Strong, broad | 9 | 2·50 | Medium, broad |
| 3 | 6·35 | Medium, sharp * | 10 | 2·27 | Medium, broad |
| 4 | 5·31 | Weak, sharp | 11 | 2·04 | Weak, diffuse |
| 5 | 4·54 | Strong, broad | 12 | 1·83 | Weak, diffuse |
| 6 | 3·80 | Strong, broad | 13 | 1·62 | Very weak, diffuse |
| 7 | 3·29 | Very weak, sharp | 14 | 1·45 | Very weak, diffuse |

* Possible superposition of two rings, one sharp, one diffuse.

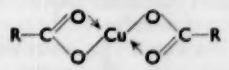
of its high intensity is attributed to a side spacing. The position and intensity of line 6 indicate that it also is due to a side spacing. By comparison with lauric acid these side spacings show that the hydrocarbon chains are close-packed in copper laurate. The calculated length of a copper laurate molecule is 35·3 Å. From the size of the long spacing (31·9 Å) it is clear that the chains must be inclined at an angle of 64·5° to the basal plane.

## DISCUSSION

*Copper Carboxylates.*—Magnetic measurements on copper carboxylates have been reported by a number of workers.[11] In all these instances measurements were made at one temperature only. Measurements over a range of temperature have been reported by

[10] Guha, *Proc. Roy. Soc.*, 1951, *A*, **206**, 353.
[11] Bhatnagar, Singh, and Ghani, *Indian J. Phys.*, 1932, **7**, 323; Amiel, *Compt. rend.*, 1938, **207**, 1097; Ploquin and Vergneau, *ibid.*, 1951, **232**, 2439; Amiel, Ploquin, and Dixmier, *ibid.*, p. 2097; Vergneau, *ibid.*, 1951, **233**, 164; Ploquin, *Bull. Soc. chim. France*, 1951, **18**, 757.

Guha [10] (acetate) and Gilmour and Pink [1] (laurate). As for both copper laurate and copper acetate the susceptibility of copper stearate decreases sharply below room temperature. In view of the striking similarity of the magnetic behaviour of the long-chain compounds to that of copper acetate (Fig. 1) it seems probable that the explanation advanced by Bleaney [12] in connection with the acetate is generally applicable. According to Bleaney, isolated pairs of copper ions are coupled together strongly by exchange forces. The two electron spins interact to form a triplet state, in which the spins are parallel ($S = 1$) and a state with the spins antiparallel ($S = 0$). The former would be paramagnetic, the latter diamagnetic. If the former state lies higher in energy by about 450 $k$ the drop in susceptibility at low temperatures can be accounted for by the pairs of ions draining out of the paramagnetic state into the diamagnetic state. Unequivocal support for this idea of interaction between pairs of copper atoms was provided by van Niekerk and Schoening's *X*-ray examination of copper acetate.[13] They showed that the molecule of copper acetate is binuclear with a Cu–Cu distance of only 2·64 Å (Fig. 4*a*). Each of the copper atoms is coplanar with four oxygen atoms arranged in a square. The magnetic evidence suggests strongly that this is also basically the structure of the laurate and stearate. In the light of this it is of interest to review previous ideas on the structure of the long-chain copper carboxylates. The earliest structure (I) was proposed in 1924 by French and Lowry [14] to account for the covalent nature of these compounds. Sidgwick [15] criticized this structure

(I)  R·CO·O·Cu·O·CO·R (II)

on the basis that the evidence did not necessarily indicate chelation and could be explained equally by the structure (II). Neither structure provides a means whereby exchange interaction may readily occur between the copper atoms, since their closest distance of approach will in either case be limited by the van der Waals radius [16] of the methylene group, to approximately 4 Å. In the van Niekerk and Schoening structure, on the other hand, the separation of the copper atoms is determined essentially by the oxygen–oxygen separation, which [17] is of the order of 2·2 Å.

While the close similarity in magnetic properties between the acetate and the laurate suggests strongly that the latter also has a binuclear structure permitting close approach of the copper atoms it is clear that the structures of the acetate and the laurate are not identical. Cupric acetate exists only in the hydrated form and in the van Niekerk and Schoening structure (Fig. 4*a*) the water molecules complete the six-fold co-ordination of the copper. Copper laurate and copper stearate on the other hand are anhydrous. A possible structure for the long-chain compounds which retains the basic binuclear structure of the acetate is illustrated in Fig. 4*b*. This permits close packing of the hydrocarbon chains as required by the *X*-ray data but in contrast to the acetate contains five-co-ordinated copper. Structures containing five-co-ordinated metal atoms have recently been postulated for terpyridyl complexes of copper, zinc, and cadmium,[18] for the pent-ammino-type copper complex $[Cu\ en_2NH_3]^{++}$ formed by the diethylenediaminecupric ion in strongly ammoniacal solution [19] and for a number of complexes of palladium and platinum.[20] Confirmation of the structure shown in Fig. 4*b* requires a full crystallographic examination.

*Carboxylates of Nickel, Cobalt, and Iron.*—Neither nickel nor cobalt long-chain carboxylates show deviations from a Curie–Weiss law in the range of temperature investigated (Fig. 2) and so, presumably, have conventional structures.

The bond character of the nickel compounds remains uncertain despite the assertion of Amiel, Ploquin, and Dixmier [11] that the magnetic results demonstrate the electrovalent

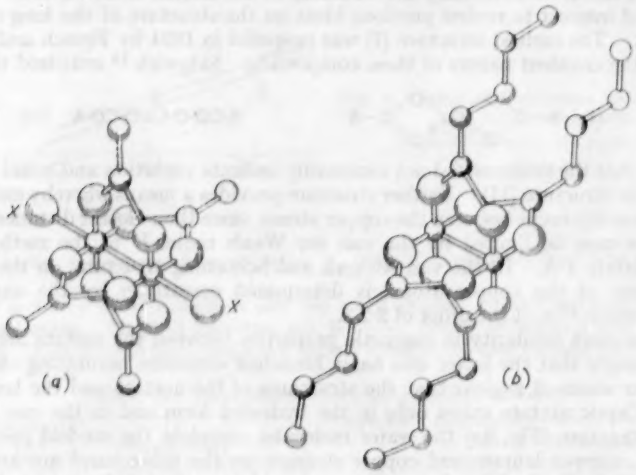
[12] Bleaney, *Rev. Mod. Phys.*, 1953, **25**, 161; Bleaney and Bowers, *Proc. Roy. Soc.*, 1952, *A*, **214**, 451.
[13] van Niekerk and Schoening, *Acta Cryst.*, 1953, **6**, 227.
[14] French and Lowry, *Proc. Roy. Soc.*, 1924, *A*, **106**, 489.
[15] Sidgwick, "Electronic Theory of Valency," Oxford Univ. Press, 1946, p. 254.
[16] Pauling, "Nature of the Chemical Bond," Oxford Univ. Press, 2nd edn., 1950, p. 190.
[17] Robertson and Woodward, *J.*, 1936, 1817.
[18] Corbridge and Cox, *J.*, 1956, 594.
[19] Bjerrum, *Acta Chem. Scand.*, 1948, **2**, 297.
[20] Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127.

character of these soaps. Magnetic results alone are unfortunately insufficient to distinguish between ionic nickel–oxygen bonds or covalent $4s4p^3$ bonds.[21] It should be noted, however, that irrespective of whether the metal–oxygen bonds are ionic or covalent the magnetic evidence indicates tetrahedral rather than coplanar co-ordination by the oxygen atoms.

Since the spin-only value of the magnetic moment of cobaltous compounds is 3·88 B.M. it is clear that in the laurate and stearate there is a substantial orbital contribution. While this is somewhat larger than that found in many quadrivalent cobalt complexes it cannot be regarded as incompatible with a tetrahedral configuration for the anhydrous compounds. The colours of the anhydrous and the dihydrated compounds are consistent with four and six co-ordinated cobalt respectively.

FIG. 4. (*a*) *The hydrated cupric acetate molecule. The two small central circles are copper atoms. The water molecules are labelled* (×). *(After van Niekerk and Schoening.*[13])

(*b*) *Proposed structure for copper laurate. The two small central circles are copper atoms. Only the first four carbon atoms of the hydrocarbon chains are shown.*




The magnetic behaviour of the ferric carboxylates, although conforming to a Curie–Weiss law in the range of temperature investigated (Fig. 3), is nevertheless unusual. The magnetic moment is much lower than that found in typical ferric compounds, while the magnetic field constant is exceptionally large (Table 1). Such characteristics recall the complex acetates, *e.g.*, $[Fe_3(CH_3{\cdot}CO_2)_6(OH)_2]NO_3,6H_2O$ studied by Welo [22] and later by Foex, Tsai, and Wucher.[23] As in the copper soaps, the decreased moment in ferric laurate may tentatively be attributed to exchange interaction between neighbouring iron atoms in the solid state. The calculated moment on the assumption of four unpaired electrons per iron atom is 4·90 B.M. (spin only) in fair agreement with the observed value for ferric stearate (4·84) and ferric laurate (5·13). Confirmation of this conclusion requires a full *X*-ray crystallographic examination. Attempts to obtain single crystals of ferric laurate suitable for such an examination have so far been unsuccessful.

We are indebted to Miss I. Woodward, M.A., for assistance with the *X*-ray measurements and interpretation of the photographs.

THE QUEEN'S UNIVERSITY OF BELFAST. [*Received, April 16th*, 1956.]

[21] Nyholm, *Quart. Rev.*, 1953, **7**, 377.
[22] Welo, *Phil. Mag.*, 1928, **6**, 481.
[23] Foex, Tsai, and Wucher, *Compt. rend.*, 1951, **233**, 1432.

# 770. *The Gum Component of Olibanum.*

By H. El-Khadem and M. M. Megahed.

Two polysaaccharides designated I and II have been isolated from the gum component of olibanum, the gum oleoresin from *Boswellia carteri*. Polysaccharide I is neutral and composed of galactose and arabinose in equimolecular ratio. Polysaccharide II is acidic and composed of galactose and galacturonic acid in the molar ratio 2 : 1.

Olibanum, the gum oleoresin exuded from the incense tree *Boswellia*, has been extensively studied. Most of the work dealt with the chemistry of its resin and its essential oils and little is known of its gum component. Tschirch and Halbey [1] isolated an acidic gum after removing the essential oils and resinous matter by extraction with 90% alcohol. The gum was in the form of a salt containing calcium and magnesium. Malandkar [2] isolated from the Indian variety of olibanum, *Boswellia serrata*, a gum which was also acidic; on hydrolysis with 3% sulphuric acid it yielded arabinose, xylose, and galactose. The present work had as its objective the isolation of the pure gum components and a study of their structures.

Commerical East African olibanum from *Boswellia carteri* was used. The essential oils and resins were removed by ether-extraction, leaving a water-soluble gum, completely precipitated by 3 volumes of ethanol and containing 11% of inorganic matter, mainly calcium. Demineralisation with cation-exchange resin then gave an acidic gum mixture. Precipitation with 3 volumes of ethanol yielded a neutral gum, polysaccharide I (26%), and the major portion (59%) was precipitated only after further addition of 3 volumes of acetone, yielding an acidic gum, polysaccharide II. Both polysaccharides were purified by repeated precipitation with alcohol and acetone.

Polysaccharide I had $[\alpha]_D^{20}$ −14·7°. Its mean reducing power determined by the methods of Meyer, Noelting, and Bernfeld,[3] and Jendrassik and Polgar [4] was 4·1%, corresponding to an average molecular weight of 4400 (30 monosaccharide molecules). The reducing power after hydrolysis, determined as glucose by Jendrassik and Polgar's method, reached a maximum value of 99·2% after 6 hours' hydrolysis with 0·5N-hydrochloric acid. Colour reactions indicated the presence of an aldopentose and the absence of ketoses, amino-sugars, and uronic acids. Paper chromatograms of the acid hydrolysate showed spots corresponding to galactose and arabinose; the two aldoses were separated on a large scale by means of broad paper chromatograms, and were thus obtained crystalline. D-Galactose was characterised as its *N*-methyl-*N*-phenylhydrazone and phenylosazone; L-arabinose as its *N*-benzyl-*N*-phenylhydrazone and *N*-methyl-*N*-phenylhydrazone. By using known amounts of hydrolysate and Meyer, Noelting, and Bernfeld's [3] and Jendrassik and Polgar's [4] methods of analysis it was shown that there were formed equimolar proportions of galactose and arabinose: after 82 hours 2·0 mols. of periodic acid were consumed and 0·22 mol. of formic acid was produced per two aldose molecules (formaldehyde could not be detected). Methylation and hydrolysis followed by fractionation on paper chromatograms yielded 2 : 4-di- (identified as aniline derivative), 2 : 3 : 4-tri- (identified as aniline derivative and phenylhydrazide), and 2 : 3 : 4 : 6-tetra-*O*-methylgalactose (identified as aniline derivative); no methylated arabinose could be isolated in crystalline form.

Polysaccharide II had $[\alpha]_D^{20}$ −9·2°. Its mean reducing power was 3·25%, corresponding to an average molecular weight of 5500 (33 monosaccharide molecules). The reducing power determined as glucose by Jendrassik and Polgar's method [4] reached a maximum value of 93% after 6 hours' hydrolysis with 0·5N-hydrochloric acid. Colour reactions indicated the presence of uronic acid and absence of ketoses, amino-sugars, and pentoses.

[1] Tschirch and Halbey, *Arch. Pharm.*, 1898, **236**, 487.
[2] Malandkar, *J. Indian Inst. Sci.*, 1925, **8**, *A*, 240.
[3] Meyer, Noelting, and Bernfeld, *Helv. Chim. Acta*, 1948, **31**, 103.
[4] Jendrassik and Polgar, *Biochem. Z.*, 1940, **304**, 271.

Paper chromatograms of the acid hydrolysate of polysaccharide II showed spots corresponding to galactose and uronic acid. The two components were separated and D-galactose was identified as above. Galacturonic acid was identified as brucine salt and by conversion into mucic acid. The galactose was estimated after quantitative separation on paper chromatograms and galacturonic acid by titration and by estimation of carbon dioxide produced on decarboxylation with 12% hydrochloric acid.[5] The ratio of galactose and galacturonic acid was found to be 2 : 1. Polysaccharide II consumed 3·0 mols. of periodic acid in 56 hours and 0·46 mol. of formic acid was produced per 3 monosaccharide molecules (formaldehyde could not be detected).

Methylation and hydrolysis followed by fractionation on paper chromatograms yielded the same methylated galactose derivatives as from polysaccharide I, suggesting the same type of galactose linkage. No methylated derivative of galacturonic acid could be isolated in a crystalline form. In both polysaccharides the amount of 2 : 4-di-*O*-methylgalactose isolated was considerable, suggesting highly branched structures.

Malandkar [2] claimed the presence of xylose in the hydrolysate of his gum; paper chromatography of polysaccharide I and II and of the crude gum showed no traces of this pentose. The xylose present in Malandkar's gum is due either to parts of the plant remains present in commercial olibanum or to a difference in the composition of the gum obtained from the Indian variety and our East African variety.

## Experimental

*Isolation and Purification of the Gum Mixture.*—Continuous extraction of powdered olibanum (160 g.) with ether for 26 hr. completely removed the essential oil and the resin components, leaving a residue (42 g.) of a white water-soluble gum. This was dissolved in warm water (900 ml.), and a small insoluble residue (mainly bark and plant remains) was rejected. The clear brown filtrate was treated with 3 vols. of ethanol and kept overnight at 0° and the precipitate collected by centrifugation. This product was again dissolved in warm water (500 ml.), filtered, and precipitated with 3 vols. of ethanol to give a colourless gum mixture (33·5 g.) containing 11% of ash.

*Separation of the Two Polysaccharides.*—A solution of the gum mixture (29 g.) in water (250 ml.) was passed several times through Zeocarb. Polysaccharide I was precipitated from the solution by the addition of 3 vols. of ethanol and collected by centrifugation after storage overnight at 0°, yielding 7·6 g. of a pale brown glass, extremely difficultly soluble in water but readily soluble in dilute alkalis.

The supernatant liquid from the alcohol precipitation was treated with 3 times its volume of acetone and kept overnight at 0°. The precipitated polysaccharide II was a colourless glass (17 g.), readily soluble in water.

Both products still contained a small amount of ash.

*Polysaccharide I.*—(a) *Purification.* A solution of polysaccharide I (7·6 g.) in 0·5N-sodium hydroxide (80 ml.) under nitrogen was acidified with acetic acid, filtered from a small insoluble residue (which was rejected), and treated with 3 vols. of ethanol. The precipitate was collected by centrifugation after storage overnight at 0°. It was treated twice more in the above manner, the last time with 5 vols. of ethanol. The final product was dialysed at 0° against frequent changes of distilled water until free from acetate ions and evaporated to dryness. Pure polysaccharide I was a pale cream-coloured friable glass, difficult to dissolve in water. It had $[\alpha]_D^{20} = -14{\cdot}7°$ (*c*, 1·09 in 1 : 3 pyridine–water) and gave no ash on combustion [Found : C, 44·8, 44·7; H, 6·3, 6·3; N, 0·0. $(C_6H_{12}O_6 + C_5H_{10}O_5)_{15} - (H_2O)_{29}$ requires C, 44·7; H, 6·1%].

(b) *Reducing power before and after hydrolysis.* (1) By the method of Meyer, Noelting, and Bernfeld.[5] The reference sugar curve for glucose was made by treating standard solutions (3 ml.) containing 0·6—2·0 mg. of glucose with 1·5% aqueous 3 : 5-dinitrosalicylic acid (1 ml.) and 6N-sodium hydroxide (1 ml.) and heating them in a thermostat at 65° for 30 min. On cooling, 10 ml. of water were added and the colour determined in a Spekker absorptiometer (a 1-cm. cell and Ilford Spectrum Green Filter No. 604).

The reducing power of polysaccharide I before hydrolysis was determined on 3 ml. of solutions

[5] Norris and Resch, *Biochem. J.*, 1935, **19**, 1590.

containing 10 mg. Duplicate readings gave for the unhydrolysed polysaccharide a reducing power of 4·0%.

(2) By the method of Jendrassik and Polgar.[4] The reducing power of the unhydrolysed polysaccharide was determined directly on 10 mg. in warm water (10 ml.). For the hydrolysed polysaccharide, solutions in 0·5N-hydrochloric acid (*ca.* 1 mg./ml.) were heated at 100° in sealed tubes for different times. The tubes were cooled and the contents accurately neutralised with 0·5N-sodium carbonate and made up to 10 ml. with water. For each determination 1 ml. of this solution was used after dilution with 10 ml. of water. Results were :

| Time (hr.) ..... | 0 | 1 | 2 | 3 | 6 | 8 |
|---|---|---|---|---|---|---|
| Reducing power as glucose (%) ..... | 4·2 | 62·0 | 80·6 | 97·7 | 99·2 | 99·2 |

(c) *Paper chromatography of hydrolysate.* The polysaccharide (40 mg.) was hydrolysed for 6 hr. at 100° in a sealed tube with 0·5N-sulphuric acid. Sulphate ions were removed by boiling the mixtures with excess of barium carbonate, and the filtrate was evaporated to dryness and redissolved in 0·5 ml. of water. One-dimensional paper chromatograms were run on Whatman No. 1 filter paper and developed with the upper layer of butan-1-ol–ethanol–water–ammonia (40 : 10 : 49 : 1),[6] and sprayed with ammoniacal silver nitrate.[7] For complete separation of the components, the chromatograms were allowed to run for 48 hr.; two spots were obtained with $R_F$ 0·14 and 0·19, controls on the same paper showing identical values for galactose and arabinose respectively.

(d) *Separation of the sugar components of hydrolysate.* The polysaccharide (0·5 g.) was hydrolysed with 0·5N-sulphuric acid (4 ml.) as above and the products were redissolved in 1·2 ml. of water. One-dimensional paper chromatograms were run on Whatman No. 1 filter paper with the hydrolysate evenly distributed along the whole length of the line of origin (0·1 ml./10 cm.); they were left to run for 48 hr. with the developing solvent mixture described in (c). Three strips, each 1 cm. wide, were cut through the length of each chromatogram in its right, left, and middle portions and sprayed with ammoniacal silver nitrate. The positions of sugar bands thus revealed were marked on the unsprayed portions of the chromatograms, which were cut off and eluted with water. Combined eluates from the upper bands gave, on drying in a vacuum-desiccator, crystals of galactose, m. p. 117° (lit., 118°), and those from the lower bands gave arabinose, m. p. 155—156·5°.

(e) *Identification of galactose.* Galactose obtained from the combined upper bands was recrystallised from hot alcohol, yielding colourless crystals, m. p. 164° not depressed on admixture with α-D-galactose. It had $[\alpha]_D^{20}$ +75° (*c* 0·24) (lit., +140° ⟶ 81·7°). A portion (0·1 g.) was heated in water (1 ml.) at 100° for 5 min. with acetic acid (0·5 ml.) and *N*-methyl-*N*-phenylhydrazine (5 drops). The crystals which separated, when recrystallised from alcohol, had m. p. 188—189° not depressed on admixture with D-galactose *N*-methyl-*N*-phenylhydrazone, m. p. 188—189°.

This galactose was also converted into the phenylosazone, m. p. and mixed m. p. 184°.

(f) *Identification of arabinose.* The product from the combined lower bands of the chromatograms, recrystallised from alcohol, had m. p. 157°, alone or mixed with β-L-arabinose. It had $[\alpha]_D^{20}$ +101° (final value; *c* 1 in $H_2O$) (lit., +191° ⟶ +105°). This product (0·1 g.) in water (1 ml.) was heated with *N*-benzyl-*N*-phenylhydrazine (5 drops) in acetic acid (0·5 ml.) for 1 min. in a water-bath. The product, recrystallised from alcohol, had m. p. 171° alone or mixed with L-arabinose *N*-benzyl-*N*-phenylhydrazone. The *N*-methyl-*N*-phenylhydrazone, similarly prepared and recrystallised, had m. p. and mixed m. p. 160°.

(g) *Estimation of the components.* The components were estimated after separation on paper chromatogram. The polysaccharide (125 mg.) was hydrolysed for 6 hr. at 100° with 0·5N-sulphuric acid, and the mixture neutralised with barium carbonate, filtered, and evaporated. The residue was dissolved in 0·5 ml. of water. One-dimensional paper chromatograms (22 cm. wide) were run with the hydrolysate (0·2 ml.) evenly distributed on the line of origin except for 5 cm. on each side. A drop of the hydrolysate was put in these spaces 2 cm. from the edges and the chromatograms developed for 48 hr. with the solvent mixture described in (c). The sugars were located as in the previous experiment. The aldoses were estimated by the methods of Jendrassik and Polgar[4] and Meyer, Noelting, and Bernfeld.[3] 0·1 ml. of eluate was used in the first method and 1 ml. in the second, diluted to 10 ml. and 3 ml. respectively. Standard sugars used were galactose and arabinose run on similar chromatograms. Correction was made for

[6] Hirst, Hough, and Jones, *J.*, 1949, 931.
[7] Partridge, *Biochem. J.*, 1948, **42**, 238.

loss of reducing power of these sugars after 6 hours' heating at 100° with 0·5N-sulphuric acid. The results were :

| Method | Galactose (%) | Arabinose (%) |
|---|---|---|
| Jendrassik and Polgar | 61·0 | 49·4 |
| Meyer, Noelting, and Bernfeld | 61·1 | 49·8 |

(h) *Oxidation with periodate.* Polysaccharide I (20 mg.) was dissolved in water (10 ml.); 1-ml. portions of this solution were kept at room temperature with 0·0056N-sodium periodate (5 ml.) and acetate buffer of pH 5·2 (0·5 ml.). Here and below unused periodate was determined by titration. The results, expressed in terms of units of mol. wt. 294 (1 galactose + 1 arabinsoe − 36) were :

| Time (hr.) | 1 | 3 | 5 | 23 | 32 | 48 | 72—82 |
|---|---|---|---|---|---|---|---|
| Mols. of $IO_4^-$ consumed per sugar unit | 0·5 | 0·8 | 0·9 | 1·3 | 1·8 | 1·9 | 2·0 |

For the estimation of formic acid, polysaccharide I (100 mg.) was treated in water (50 ml.) with 1·5% aqueous potassium periodate (30 ml.) and left in the dark for 96 hr. and the excess of periodate destroyed with ethylene glycol. Formic acid was titrated against 0·09N-barium hydroxide (methyl-red) : 0·22 mol. was produced per unit of mol. wt. 294.

(i) *Methylation.* Preliminary experiments with polysaccharide I showed that after 14 consecutive treatments with methyl iodide and sodium in liquid ammonia [8] the methoxyl content reached 29·9%. Methylation with dimethyl sulphate in 35% aqueous sodium hydroxide [9] 16 consecutive times gave a product having 34·0% of OMe. Partially methylated polysaccharide I (6 g.) obtained by the above two methods was acetylated with acetic anhydride and pyridine, then methylated with dimethyl sulphate in 35% aqueous sodium hydroxide.[10] The process was repeated 14 times and the product dialysed against frequent changes of distilled water until free from sulphate ions and then evaporated to dryness, giving a pale brown gum (1·35 g.) [Found : OMe, 41·2. $C_6H_7O_2(OMe)_3,C_5H_6O_3(OMe)_2$ requires OMe, 42·6%]. The methylated polysaccharide I was hydrolysed first with 1% methanolic hydrogen chloride, then with 0·5N-hydrochloric acid, finally neutralised with silver carbonate, and a portion of this hydrolysate run for 10 hr. on paper chromatograms with the solvent mixture described in (c). Three spots were obtained, having $R_g$, 0·41, 0·64, and 0·88 respectively ($R_g$ = relative to tetramethyl glucose). The methylated sugars (0·8 g.) were separated on large paper chromatograms as described in (d). Three bands were obtained; the eluate from the upper band yielded on evaporation 2 : 4-di-*O*-methylgalactose as its hydrate, m. p. 102° (77 mg.), and was converted into the aniline derivative, m. p. and mixed m. p. 212°. The eluate (88 mg.) from the second band gave on boiling with alcoholic aniline a derivative, m. p. 164—165°, identical with that from 2 : 3 : 4-tri-*O*-methylgalactose. Another portion of this band was treated with bromine water and the acid formed converted into the phenylhydrazide, m. p. 170° not depressed on admixture with 2 : 3 : 4-tri-*O*-methylgalactonic phenylhydrazide. From the third band 2 : 3 : 4 : 6-tetra-*O*-methylgalactose (35 mg.) was obtained and identified by its conversion into the aniline derivative, m. p. and mixed m. p. 184—186°.

*Polysaccharide II.*—(a) *Purification.* Polysaccharide II (7·5 g.) was passed in water (250 ml.) through Zeocarb, filtered, and treated with 3 vols. of ethanol; a small amount of polysaccharide I separated (1·5 g.) and was removed by centrifugation after storage overnight at 0°. The supernatant liquid after the alcohol precipitation was treated with 3 vols. of acetone and left overnight at 0° and the precipitated polysaccharide II collected by centrifugation and dried. On further treatment as above no precipitate separated on addition of 3 vols. of ethanol; with acetone 5·5 g. of product were obtained. For final purification this product (5 g.) was dialysed in water (100 ml.) at 0° against frequent changes of distilled water, then treated with 3 vols. of ethanol; again no precipitation occurred and the solution was treated with 5 vols. of acetone and kept overnight at 0°; pure polysaccharide II was collected by centrifugation and dried. It (4·9 g.) formed a white powder, readily soluble in water, $[\alpha]_D^{20}$ −9·2° (*c*, 1·1), [Found : C, 43·5, 43·6; H, 6·2, 6·1; N, 0·0; ash, 0·0. $(C_6H_{10}O_7 + 2C_6H_{12}O_6)_{11} - (H_2O)_{32}$ requires C, 43·1; H, 5·6%].

(b) *Reducing power before and after hydrolysis.* The reducing powder of the unhydrolysed polysaccharide II was determined by the method of Meyer, Noelting, and Bernfeld.[3] Duplicate

[8] Muskat, *J. Amer. Chem. Soc.*, 1934, **56**, 2449.
[9] Haworth, *J.*, 1915, **107**, 8.
[10] Haworth and Percival, *J.*, 1932, 2279.

readings gave a reducing power of 3·2%. The reducing power before and after hydrolysis determined by Jendrassik and Polgar's method [4] was :

| Time (hr.) | 0 | 1 | 2 | 4 | 6 | 8 |
|---|---|---|---|---|---|---|
| Reducing power as glucose (%) | 3·3 | 62·0 | 77·5 | 89·9 | 93·0 | 93·0 |

(c) *Paper chromatography of the hydrolysate.* The polysaccharide was hydrolysed and chromatographed as described for polysaccharide I. Two spots were obtained having $R_F$ values 0·03 and 0·14; controls on the same paper showed identical values for uronic acid and galactose (galacturonic and glucuronic acid showed very similar $R_F$ values and could not be separated from an artificial mixture of the two).

(d) *Separation of the sugar components of the hydrolysate.* The hydrolysis products were separated on broad paper chromatograms as described for polysaccharide I. The combined eluates from the upper bands gave, when evaporated in a vacuum desiccator, glassy galacturonic acid; those from the lower bands gave crystalline galactose.

(e) *Identification of galacturonic acid.* A portion (150 mg.) of the dry eluate from the upper bands of the chromatograms was heated in water (1 ml.) at 100° with the equivalent amount of brucine. After 15 min. the solution was cooled and extracted several times with chloroform to remove unchanged brucine. On drying of the aqueous layer in a vacuum-desiccator crystals of the brucine salt of galacturonic acid were obtained and recrystallised from alcohol. The pure salt had m. p. 176—178°, not depressed on admixture with brucine galacturonate.

The uronic acid (150 mg.) was treated in water with saturated aqueous bromine (25 ml.), left at room temperature for 4 days, and evaporated to dryness, and the residue dissolved in N-sodium hydroxide (2 ml.). Mucic acid was precipitated by addition of concentrated hydrochloric acid and, recrystallised from ethanol–ether, had m. p. and mixed m. p. 213°.

(f) *Identification of galactose.* The product obtained from the combined lower bands, recrystallised from alcohol, gave galactose, m. p. and mixed m. p. 164°, converted into the *N*-methyl-*N*-phenylhydrazone and phenylosazone as described for polysaccharide I.

(g) *Estimation of the components.* Galactose was estimated after separation on paper chromatograms as in the case of polysaccharide I (methods of Jendrassik and Polgar [4] and Meyer, Noelting, and Bernfeld [3]).

Galacturonic acid was estimated by Norris and Resch's method.[5] The polysaccharide (97 mg.) was heated with 12% hydrochloric acid at 140—150° under nitrogen, and the carbon dioxide evolved absorbed in N-barium hydroxide. The amount of carbon dioxide, from the decarboxylation of the uronic acid, was determined by titrating the barium hydroxide with 0·1N-acid. Further, galacturonic acid in the polysaccharide was estimated directly by titration against standard alkali. All the results are shown in the annexed Table.

| | |
|---|---|
| Galactose : Jendrassik and Polgar | 71·7% |
| Meyer, Noelting, and Bernfeld | 70·1% |
| Galacturonic acid : Norris and Resch | 38·0% |
| Titration | 39·1% |

(h) *Oxidation with periodate.* This was conducted as for polysaccharide I. The results expressed in terms of sugar units of mol. wt. 500 (2 galactose + 1 galacturonic acid − 54) were :

| Time (hr.) | 1 | 4 | 6 | 10 | 14 | 24 | 44—56 |
|---|---|---|---|---|---|---|---|
| Mols. of $IO_4^-$ consumed per sugar unit | 0·3 | 0·9 | 1·1 | 1·6 | 1·8 | 2·4 | 3·0 |

Polysaccharide II (175 mg.) in water (50 ml.) was treated with 1·5% potassium periodate solution (30 ml.), left in the dark for 60 hr., and treated with ethylene glycol. Formic acid was titrated against 0·09N-barium hydroxide (methyl-red); 0·46 mol. of formic acid was produced per sugar unit of mol. wt. 500.

(i) *Methylation.* Polysaccharide II (2·5 g.) was methylated as was polysaccharide I. The final methylated product had OMe, 45·9% [$C_6H_5O_3(OMe)_3$,$2C_6H_7O_2(OMe)_3$ requires OMe, 44·6%]. The methylated polysaccharide II (1·1 g.) was hydrolysed and the products were separated on large paper chromatograms as described for polysaccharide I. Three bands were obtained : the eluate from the upper band yielded on evaporation 2 : 4-di-*O*-methylgalactose as its hydrate, m. p. 102° (73 mg.), and was converted into the aniline derivative, m. p. and mixed m. p. 212°. The eluate from the second band (117 mg.) gave with boiling alcoholic aniline a derivative, m. p. 164—165°, identical with that from 2 : 3 : 4-tri-*O*-methylgalactose : another portion of this band was converted by bromine water, etc., into the phenylhydrazide, m. p. 170° alone or mixed with that of 2 : 3 : 4-tri-*O*-methylgalactonic acid. From the third

band 2 : 3 : 4 : 6-tetra-*O*-methylgalactose (96 mg.) was obtained and identified by its conversion into the aniline derivative, m. p. and mixed m. p. 184—186°.

The authors thank Professor E. L. Hirst for authentic specimens of the methylated galactose derivatives, Professor H. N. Rydon for valuable suggestions, and Professors G. Soliman and M. Omar for their interest.

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## 771. *A Kinetic Study of the Alkaline Hydrolysis of Some Aliphatic Esters.*

By J. D. R. THOMAS and H. B. WATSON.

Velocities and Arrhenius activation energies have been determined for the alkaline hydrolysis of the ethyl esters of ten olefinic acids in 85% alcohol. The results can be understood in the light of the inductive effects of alkyl groups, mesomeric effects in cases where a double bond is conjugated with the ethoxycarbonyl group, and hyperconjugation in suitable structures. Earlier results, some of which have been redetermined, for the alkaline hydrolysis of saturated aliphatic esters are also discussed.

EVANS, GORDON, and WATSON,[1] and Smith and Levenson,[2] determined bimolecular velocity coefficients and Arrhenius activation energies for the alkaline hydrolysis of the ethyl esters of a series of saturated aliphatic acids in 85% alcohol. No similar investigation of the hydrolysis of unsaturated esters has hitherto been conducted, however. We now further consider the kinetics of alkaline hydrolysis of the saturated esters, and describe an extension of the work to ten unsaturated esters. The results are analysed on the basis of the kinetic equation $k = PZe^{-E/RT}$, the new experimental results being summarised in Table 1.

TABLE 1. *Alkaline hydrolysis of esters in 85% alcohol.*

| Ester | $10^3k_{25}$ | $10^3k_{40}$ | $10^3k_{55}$ | $10^3k_{65}$ | $E$ (cal./mole) | $\log_{10} PZ$ |
|---|---|---|---|---|---|---|
| Acetic [a] | 6·98 | 23·0 | — | — | 14,700 [b] | 8·6 |
| Propionic | 3·65 | 11·7 | 33·9 | — | 14,500 [c] | 8·2 |
| Trimethylacetic | — | 0·107 | 0·248 | 0·814 | 17,100 [d] | 8·0 |
| Acrylic | 4·67 | 16·3 | 49·7 | — | 15,400 | 8·9 |
| But-3-enoic [e] | 3·63 | 11·6 | 33·8 | — | 14,500 | 8·2 |
| Pent-4-enoic | 3·62 | 11·8 | 34·0 | — | 14,500 | 8·2 |
| Crotonic | 0·625 | 2·34 | 7·95 | — | 16,500 | 8·9 |
| β-Methylcrotonic [f] | — | 0·322 | 1·19 | 2·71 | 18,000 | 9·0 |
| Non-2-enoic | 0·660 | 2·36 | 7·64 | — | 15,900 | 8·5 |
| Penta-2 : 4-dienoic | 1·42 | 5·50 | 18·8 | — | 16,800 | 9·5 |
| Sorbic | 0·473 | 1·96 | 7·11 | — | 17,600 | 9·6 |
| α-Methylacrylic | 0·933 | 3·30 | 10·9 | — | 16,000 | 8·7 |
| Tiglic | — | 0·563 | 1·96 | 4·29 | 17,100 | 8·7 |

[a] A determination at 20° gave $10^3k = 4·54$. [b] Confirms Smith and Levenson.[2] [c] Confirms Evans, Gordon, and Watson.[1] [d] Confirms Evans, Gordon, and Watson (recalc.). [e] Values for first 10% of reaction; see p. 3963. [f] A determination at 70° gave $10^3k = 4·04$.

*Discussion.—Alkaline hydrolysis of saturated esters.* The rather weak electron-repelling character of alkyl groups (+*I* effect) renders the attack of the negative ion progressively more difficult, leading to an increasing value of the energy of activation, both as the chain of the ester becomes longer, and in series such as $CH_3{\cdot}CO_2Et < CH_2R{\cdot}CO_2Et < CHR_2{\cdot}CO_2Et < CR_3{\cdot}CO_2Et$ (compare instances cited by Evans, Gordon, and Watson [1]). The magnitude of this inductive effect falls off very rapidly as the substituent alkyl group is moved further from ethoxycarbonyl, and accordingly Evans, Gordon, and Watson [1] found that the energy of activation for alkaline hydrolysis rose from acetic to butyric ester, beyond

[1] Evans, Gordon, and Watson, *J.*, 1938, 1439.
[2] Smith and Levenson, *J. Amer. Chem. Soc.*, 1939, **61**, 1172.

which only minor and irregular variations occurred in the *n*-acid esters. The value of *E* rose quite sharply with substitution of methyl groups in the α-position, however, and this was interpreted as a manifestation of the inductive effects of the methyl groups. In Table 2 values of *E* recorded by Evans, Gordon, and Watson, and by Smith and Levenson, certain of them confirmed or modified in the present work, are classified in accordance with the number of alkyl groups which are substituted at the α- and β-positions, the effect of substitution beyond the β-position being negligible.

Table 2 shows that, in the main, the energies of activation are determined by the number of alkyl groups present at the α- and β-positions, but three peculiarities call for comment. (1) An appreciable rise in *E* would be expected in passing from acetic to propionic ester

TABLE 2. *Energies of activation for alkaline hydrolysis of saturated esters in 85% alcohol.*

| Number of α- and β-substitutions | Position | Ester | *E* (cal./mole) | Ref. |
|---|---|---|---|---|
| 0 | — | $CH_3 \cdot CO_2Et$ | 14,700 | 2 [a] |
| 1 | α | $CH_3Me \cdot CO_2Et$ | 14,500 | 1 [a] |
| 2 | 2α | $CHMe_2 \cdot CO_2Et$ | 15,000 | 1 [b] |
| | 1α, 1β | $CH_2Me \cdot CH_2 \cdot CO_2Et$ and higher *n*-esters | 15,000 | 1 |
| 3 | 1α, 2β | $CHMe_2 \cdot CH_2 \cdot CO_2Et$ | 15,700 | 1 |
| | 1α, 2β | $CHMeEt \cdot CH_2 \cdot CO_2Et$ | 15,700 | 3 |
| | 2α, 1β | $CH_2Me \cdot CHMe \cdot CO_2Et$ | 15,600 | 1 [c] |
| | 3α | $CMe_3 \cdot CO_2Et$ | 17,100 | 1 [d] |
| 4 | 2α, 2β | $CHEt_2 \cdot CO_2Et$ | 17,300 | 1; 3 |
| | 2α, 2β | $CHPr_2 \cdot CO_2Et$ | 17,200 | 3 |
| | 2α, 2β | $CHBu_2 \cdot CO_2Et$ | 17,700 | 3 |

[a] Confirmed in present work. [b] Recalc. by Davies and Evans, *J.*, 1940, 339. [c] Recalc. in present work. [d] Recalc. and confirmed experimentally in present work.

(one α-substitution), but such is not found. (2) Substitutions at the α- and β-positions have similar effects, *viz.*, a rise of 500 to 700 cal. for each substitution, in spite of the weakening of the inductive effect by interposition of a saturated carbon atom. (3) The effect of substituting a *third* methyl group at the α-position is much greater than that produced by the first two substitutions, the value of *E* for ethyl trimethylacetate being 2000 cal. higher than for ethyl *iso*butyrate and 1500 cal. higher than for ethyl α-methylbutyrate where the third substitution is in the β-position. The esters of the last group (two α- and two β-substitutions) also show unusually high energies of activation.

The first two of the peculiarities noted above may be understood in the light of hyperconjugation, which will be exhibited by any ester having one or more α-hydrogen atoms, and will oppose the attack of the nucleophilic reagent. In ethyl acetate there are three hydrogen atoms available for this process and an appreciable increase in the energy of activation must result. In ethyl propionate, however, with only two α-hydrogen atoms, there will be less hyperconjugation, and the decrease in this effect may well balance the inductive effect of the α-methyl group, leaving the value of *E* not very different from that for ethyl acetate. In the other esters, also, α-substitution involves the loss of one hydrogen atom capable of participating in hyperconjugation, and hence the *total* effect of α-substitution becomes no greater than that of β-substitution where the inductive effect of the β-alkyl group is reduced by passage through a saturated carbon atom.

The structure of trimethylacetic ester may be compared with that of the *neo*pentyl halides, $CMe_3 \cdot CH_2X$, as pointed out by Dostrovsky, Hughes, and Ingold,[4] who showed that the very low rates of bimolecular ($S_N2$) substitution in these halides were to be ascribed to steric retardation. It is reasonable to conclude that the same phenomenon is responsible for the unusually high energy of activation observed in the hydrolysis of ethyl trimethylacetate, although, as Dostrovsky, Hughes, and Ingold have explained, the retardation of ester hydrolysis will not be so powerful as that found in the *neo*pentyl compounds because

[3] Levenson and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 1556.
[4] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 173.

the unsaturation of the ethoxycarbonyl group allows a transition state with only four groups attached to the seat of substitution. It appears very probable, however, that the same factor operates in the two cases and also, perhaps, in the alkaline hydrolysis of diethyl-, dipropyl-, and dibutyl-acetic ester which also show high energies of activation. Suggestions on these lines have been made previously; thus, Smith [5] recognised the possibility of steric retardation in some cases of esterification and hydrolysis, and still earlier Hinshelwood and Legard [6] expressed doubt as to whether the slow rate of esterification of trimethylacetic acid could be interpreted on the basis of polar effects alone.

*Alkaline hydrolysis of unsaturated esters.* The olefinic linkage has electron-attractive characters, usually denoted by $-I$, and this is illustrated by the enhanced strengths of acrylic, but-3-enoic, and pent-4-enoic acid as compared with the corresponding saturated acids.[7] Relatively to the βγ- and γδ-double linkages, however, the αβ-double bond in acrylic acid has an effect which is smaller than would be expected, and Dippy [7] has suggested that there is an opposing mesomeric effect in cases where the double bond is conjugated with the carboxyl group. The values of the energies of activation for the alkaline hydrolysis of acrylic, but-3-enoic, and pent-4-enoic ester have now given a very clear demonstration of the existence of an effect opposite in sign to the inductive effect of the olefinic linkage. In ethyl acrylate, the value (15,400 cal./mole) is nearly a thousand calories *higher* than that for ethyl propionate (14,500 cal./mole), whereas the inductive effect of the unsaturated grouping would cause a decrease. On the other hand, the energies of activation for the hydrolysis of the βγ- and γδ-unsaturated esters are somewhat *lower* than those for the corresponding saturated esters (14,500 cal./mole, which, for ethyl but-3-enoate is a maximum value, see p. 3963, against 15,000 for the saturated esters), in accordance with the $-I$ effect of the double linkage. Similar phenomena were observed by Levenson and Smith [8] in their comparison of the alkaline hydrolysis of α-, β-, γ-, and δ-phenyl-substituted esters with that of ethyl benzoate.

*β-Methyl substitution in ethyl acrylate.* The inductive effect of the olefinic linkage and the conjugation of the double bond with ethoxycarbonyl are also present in crotonic and β-methylcrotonic ester, but these have in addition one and two methyl groups respectively, substituted at the β-position. By analogy with the saturated esters considered above, the presence of these methyl groups would be expected to lead to increments of about 600 and 1200 cal./mole, respectively, in the energy of activation for alkaline hydrolysis. The observed increases are much greater, however, *viz.*, 1100 and 2600 cal./mole. The relevant figures, with those of the corresponding saturated esters, are as follows:

| | | | | | |
|---|---|---|---|---|---|
| Acrylic ..... | 15,400 | Crotonic ..... | 16,500 | β-Methylcrotonic ..... | 18,000 |
| Propionic..... | 14,500 | Butyric ..... | 15,000 | *iso*Valeric ..... | 15,700 |

The additional factor responsible for these larger energies of activation is probably hyperconjugation, for which the β-methyl group in crotonic ester and the *two* methyl groups in β-methylcrotonic ester are suitably placed. The same effect may account for the fall in the dissociation constants of the acids,[7] the values of $10^5K$ being as follows: acrylic, 5·56; crotonic, 2·03; β-methylcrotonic, 0·76.

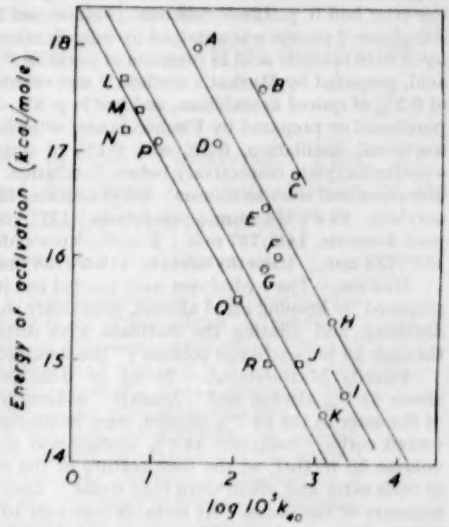
For an ester with a lengthened chain, *viz.*, ethyl non-2-enoate, the energy of activation (15,900 cal./mole) lies between the values for acrylic and crotonic ester, and a contributory factor is probably the reduction of hyperconjugation by replacement of the $-CH_3$ of crotonic ester by $-CH_2-$, but the longer chain may introduce other factors also. For ethyl penta-2:4-dienoate (16,800 cal./mole) and ethyl sorbate (17,600) the energies of activation are considerably higher than for ethyl acrylate, and it would appear that the extended conjugation brings out the mesomeric effect more powerfully, while in sorbic ester hyperconjugation may be considerable.

*α-Methyl substitution in ethyl acrylate.* For the alkaline hydrolysis of α-methylacrylic

[5] Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 1139.
[6] Hinshelwood and Legard, *J.*, 1935, 1588.
[7] Dippy, *Chem. Rev.*, 1939, **25**, 180.
[8] Levenson and Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 2324.

and tiglic ester, the energies of activation (16,000 and 17,100 cal./mole, respectively) are 600 cal./mole higher than for ethyl acrylate and crotonate, and this is the increment produced by substitution of one methyl group in the α- or β-position of a saturated ester and ascribed above to the inductive effect of methyl. Comparison of the values for ethyl α-methylacrylate and ethyl tiglate shows a difference of 1100 cal./mole, identical with that found for acrylic and crotonic ester, and doubtless to be ascribed to the same factors. Thus, no new or unexpected influences are revealed in the α-substituted esters.

*Variations in the non-exponential term of the kinetic equation.* The above discussion of the effects of structural changes in R upon the alkaline hydrolysis of esters $R{\cdot}CO_2Et$ has been based upon the values of the energy of activation. The changes in $E$ are in some cases accompanied by variations in the $PZ$ term of the kinetic equation. These differences are not large, however, and it would be unwise to draw detailed conclusions from them; but the general tendency is in harmony with that which would be expected on the basis of mesomeric and hyperconjugative effects. The variations in $PZ$ are illustrated in the




*Plot of energy of activation against* $\log_{10} k_{40}$, *illustrating values of* $PZ$.

□ *From results of Evans, Gordon, and Watson,*[1] *or Levenson and Smith.*[3]

*Acids: A, β-methylcrotonic; B, sorbic; C, penta-2:4-dienoic; D, tiglic; E, crotonic; F, α-methylacrylic; G, non-2-enoic; H, acrylic; I, acetic; J, butyric and higher n-acids; K, propionic, but-3-enoic, pent-4-enoic; L, dibutylacetic; M, diethylacetic; N, dipropylacetic; P, trimethylacetic; Q, α-methylbutyric; R, isobutyric.*

Figure, where values of $E$ are plotted against $\log_{10} k_{40}$, and the straight lines have the theoretical slope $-2{\cdot}303RT$: that is, points lying on the same straight line indicate equal values of $PZ$.

The relevant observations are as follows. (*a*) Evans, Gordon, and Watson found that lengthening of the chain in the *n*-acid esters beyond ethyl propionate led to no change in $PZ$, and we have now observed that a double bond at the βγ- or γδ-position does not change this factor. In these cases, neither mesomeric nor hyperconjugative effects are involved. (*b*) Branching at the α-carbon atom leads to a small decrease in $PZ$, as shown by the following values of $\log_{10} PZ$: acetate, 8·6; propionate and higher *n*-acid esters (calculated from the results of Evans, Gordon, and Watson), 8·2—8·3; *iso*butyrate, α-methylbutyrate, diethyl-, dipropyl-, and dibutyl-acetate (calc. from results of Evans, Gordon, and Watson and of Smith and Levenson), and trimethylacetate, 7·8—8·0. The differences are small, but may be due to the successive removal of α-hydrogen atoms, leading to less hyperconjugation. (*c*) An αβ-double bond raises $\log PZ$ to an appreciable extent; *e.g.*, for acrylic, crotonic, and β-methylcrotonic ester it has a value of 8·9—9·0, and it is difficult to resist the conclusion that the mesomeric effect is responsible in these cases where the double bond is conjugated with the ethoxycarbonyl group. Moreover, in penta-2:4-dienoic and sorbic ester, where the energy of activation has already indicated that this effect is more

powerful in the extended conjugated system, the *PZ* factor is increased further (log *PZ* = 9·5). In α-methylacrylic and tiglic ester, with branching at the α-carbon, there is an indication of a falling *PZ* (log *PZ* = 8·7), and a rather larger fall in non-2-enoic ester (log *PZ* = 8·5) may be connected with the influences already referred to.

In view of the relatively small differences concerned, these comments upon the values of the non-exponential factor are merely tentative; the effect of an α,β-double bond on the value of *PZ* is doubtless a real one, however.

Results recently reported by Humphreys and Hammett [9] for the alkaline hydrolysis of ethyl formate place this ester in a unique position, as would be expected from other known facts such as the relatively high dissociation constant of formic acid.

## Experimental

*Materials.*—But-3-enoic acid, prepared by hydrolysis of allyl cyanide with concentrated hydrochloric acid,[10] was esterified by the Fischer–Speier method and after fractional distillation the ester had b. p. 124·5°/768 mm. (Falaise and Frognier [11] give b. p. 124·2—124·4°/761·5 mm.). Ethyl non-2-enoate was obtained by esterification of the acid got by condensation of *n*-heptaldehyde with malonic acid in presence of pyridine,[12] and had b. p. 118°/12 mm. Penta-2:4-dienoic acid, prepared by Muskat's method,[13] was esterified by the Fischer–Speier method in presence of 0·3% of quinol as stabiliser, and had b. p. 57—57·5°/13 mm. The remaining esters were either purchased or prepared by Fischer–Speier esterification of the appropriate acids, and purified by fractional distillation, 0·3% and 0·1% of quinol being added to ethyl acrylate and ethyl α-methylacrylate respectively before distillation. The b. p.s agreed well with those found in the literature and were as follows: ethyl acetate, 76·9—77·2°/760 mm.; propionate, 99°/755 mm.; acrylate, 99·5°/758 mm.; crotonate, 137°/756 mm.; α-methylacrylate, 117·5°/752 mm.; pent-4-enoate, 144°/767 mm.; β-methylcrotonate, 61·5°/30 mm.; sorbate, 85°/20 mm.; tiglate, 156°/758 mm.; trimethylacetate, 118·5°/758 mm.

*Medium.*—The hydrolyses were carried out in 84·7% ethyl alcohol, of $d_4^{20}$ 0·8316. This was prepared by keeping ethyl alcohol, previously shaken with silver oxide, over freshly baked lime, distilling, and diluting the distillate with distilled water which had been passed four times through an ion-exchange column (" Bio-deminrolit FF ").

*Velocity Measurements.*—25 ml. of 0·2N-alcoholic sodium hydroxide, prepared from the above 84·7% alcohol and " AnalaR " sodium hydroxide pellets, and 10 ml. of a 0·5M-solution of the ester in the 84·7% alcohol, were measured into separate 150 ml. conical flasks fitted with waxed corks. Sufficient 84·7% alcohol was then added to the flasks to bring the combined volume on mixing, at the temperature of the reaction, to 100 ml. The initial concentrations of both ester and alkali were thus 0·05M. Zero time was taken as the half-point of mixing the contents of the flasks. At suitable intervals 10 ml. of the mixture were withdrawn and added to 10 ml. of N/15-hydrochloric acid, and the excess of acid titrated with N/20-sodium hydroxide to bromothymol-blue. Each end-point was matched against a freshly prepared solution of 15 ml. of M/30-sodium benzoate in 15 ml. of 50% aqueous alcohol containing the same amount of indicator as in the titration. Bimolecular velocity coefficients were calculated from the equation $k_2 = (1/t)x/a(a-x)$. A typical run is tabulated.

*Hydrolysis of ethyl α-methylacrylate at* 40°. [Ester] = [NaOH] = 0·0508M.

(10 Ml. of the reaction mixture were pipetted into 10 ml. of 0·0668N-HCl, and the titration carried out with 0·0511N-sodium hydroxide.)

| Time (sec.) | 600 | 1500 | 2400 | 3600 | 4800 | 6600 |
|---|---|---|---|---|---|---|
| NaOH titre (ml.) | 4·03 | 5·11 | 5·98 | 6·86 | 7·57 | 8·36 |
| $10^3k_2$ | 3·26 | 3·26 | 3·30 | 3·28 | 3·31 | 3·31 |

Mean value of $10^3k_2$ = 3·29.

The plot of log *k* against $1/T$ gave a good straight line in each case, and hence the energies of activation were calculated.

[9] Humphreys and Hammett, *J. Amer. Chem. Soc.*, 1956, **78**, 521.
[10] Mannich, *Arch. Pharm.*, 1935, **273**, 415.
[11] Falaise and Frognier, *Bull. Soc. chim. Belg.*, 1933, **42**, 427.
[12] Knoevenagel, D.-R.P. 156,560; *Chem. Zentr.*, 1905, I, 56.
[13] Muskat, *J. Amer. Chem. Soc.*, 1930, **52**, 326.

The bimolecular velocity coefficient for ethyl but-3-enoate showed a rapid decrease as the reaction progressed, as illustrated below for 40°. The figures in the last column are calculated

| Time (sec.) | Titre (ml.) | $10^3k$ | $10^3k'$ | Time (sec.) | Titre (ml.) | $10^3k$ | $10^3k'$ | Time (sec.) | Titre (ml.) | $10^3k$ | $10^3k'$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 180 | 4·07 | 11·43 | — | 3000 | 6·13 | 2·84 | 2·33 | 9000 | 8·44 | 2·50 | 2·32 |
| 600 | 4·41 | 4·85 | — | 5400 | 7·26 | 2·58 | 2·31 | | | | |

on the basis of 600 sec. as zero time, and they are identical with the bimolecular coefficient found for ethyl crotonate (Table 1). The ethyl but-3-enoate clearly isomerises during the reaction (cf. Goldberg and Linstead [14]). The values of $k$ recorded for ethyl but-3-enoate in Table 1 are those for approximately the first 10% of the reaction. They are, of course, not as accurate as the remaining velocity coefficients, since, once the isomerisation has begun, the measured velocity is partly that of the hydrolysis of ethyl crotonate. The value of $E$ for this hydrolysis is considerably higher than that for ethyl but-3-enoate, and the figure of 14,500 cal./mole for the latter should therefore be regarded as a maximum value: the true value is probably lower.

The authors thank Mr. L. K. Pugh for assistance in the preparative work.

THE COLLEGE OF TECHNOLOGY AND COMMERCE, CARDIFF. [*Received, May 22nd,* 1956.]

[14] Goldberg and Linstead, *J.*, 1928, 2343.

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## 772. *Experiments on the Synthesis of the Pyrethrins. Part XI.* Synthesis of* cis-*Pyrethrolone and Pyrethrin I: Introduction of the* cis-*Penta-2:4-dienyl System by Selective Hydrogenation.*†

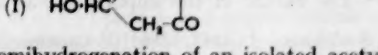
By L. CROMBIE, S. H. HARPER, and F. C. NEWMAN.

When 1 mol. of hydrogen is added to a monosubstituted vinylacetylene in the presence of a palladium catalyst, a *cis*-vinylic diene is produced. Absorption of hydrogen does not cease at this stage, even when poisoned catalysts are used, but continues until the vinyl grouping is saturated, and gives a *cis*-mono-olefin. With poisoned catalysts, gas absorption then becomes very slow. The hydrogenations are not completely selective.

Intermediates described in Part X are used in synthesis of (±)-*cis*-pyrethrolone, which is found to be identical with pyrethrolone B-2 of natural origin. The final stage in this synthesis involves controlled hydrogenation of a vinylacetylene system to produce the *cis*-diene side-chain. Improvements to our earlier synthesis of (±)-*trans*-pyrethrolone are described.

From synthetic (±)-*cis*-pyrethrolone the diastereoisomeric mixture of esters (+)-*cis*-pyrethronyl (+)-*trans*-chrysanthemate and (−)-*cis*-pyrethronyl (−)-*trans*-chrysanthemate is prepared: the former is natural pyrethrin I. Other insecticidal rethrins having pent-4-en-2-ynyl and hexa-*trans*-2:*trans*-4-dienyl side-chains are reported.

IN Part X * the preparation of potential intermediates for the synthesis of *cis*-pyrethrolone (I), containing the terminal grouping $\cdot CH_2 \cdot C{:}C \cdot CH{:}CH_2$, was described. Attention is now turned to the selective hydrogenation of these intermediates as a means of introducing the *cis*-penta-2:4-dienyl system.

(I) 

Although catalytic semihydrogenation of an isolated acetylenic bond at a supported palladium catalyst is a well-established method of introducing a *cis*-ethylenic bond, generally of good stereochemical purity,[1] the method has been less used for compounds

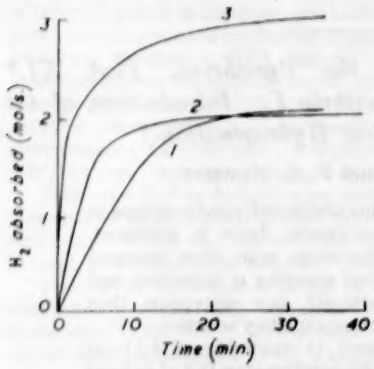
* Part X, *J.*, 1956, 126.

† Read in abstract at the XIVth Internat. Congr. Pure and Applied Chemistry, Zürich, July, 1955.

[1] Campbell and Campbell, *Chem. Rev.*, 1942, **31**, 77; Crombie, *Quart. Rev.*, 1952, **6**, 101.

containing the acetylenic bond conjugated with an ethylenic bond. Evidence has accumulated that in the hydrogenation of such enyne systems reduction continues beyond the uptake of 1 mol. of hydrogen and even if reduction is interrupted at this point the diene is contaminated with unchanged enyne and oversaturated material.[2] A further complication is associated with the substituted vinylacetylenes with which we are concerned. Lebedev, Kobliansky, and Yakubchik,[3] using platinum black, and Dupont,[4] using Raney nickel as catalyst, showed that monosubstituted olefins, R·CH:$CH_2$, are reduced much more rapidly than more substituted olefins. If this reduction of a vinyl group were to occur (over a supported palladium catalyst) concurrently with semihydrogenation of the acetylenic linkage, then the difficulty in isolating a pure *cis*-diene from partial reduction of the ·$CH_2$·C:C·CH:$CH_2$ system might be even greater than for the system ·$CH_2$·C:C·CH:CH·$CH_2$·.

To examine the efficacy of supported palladium catalysts in the selective hydrogenation of the ·$CH_2$·C:C·CH:$CH_2$ system, the reduction of oct-7-en-5-yn-2-one, its semicarbazone, and hept-6-en-4-ynoic acid [5] was studied. In all three cases, when the poisoned catalysts of Isler *et al.*[6] and of Lindlar [7] were used, 2 mols. of hydrogen were absorbed without appreciable change in rate of uptake. Absorption then practically ceased. Even with palladised barium sulphate, absorption of the third mol. of hydrogen occurred more slowly




*Hydrogenation of oct-7-en-5-yn-2-one semicarbazone using (1) Isler catalyst, (2) Lindlar catalyst, and (3) palladium–barium sulphate catalyst.*

than that of the first 2 mols. (see Figure). By increasing the proportion of quinoline to Lindlar catalyst the rate of absorption was slowed but there was no break in the curve when 1 mol. of hydrogen had been absorbed.

As most of the ketones and acids that might result from the hydrogenation of oct-7-en-5-yn-2-one and hept-6-en-4-ynoic acid were available from our earlier work, it has been possible to identify the products formed on absorption of 1 and 2 mols. of hydrogen and hence deduce the course of reduction. We find, in agreement with Lebedev *et al.* and Dupont, that oct-7-en-2-one, a monosubstituted olefin, is reduced more rapidly than oct-*trans*-5-en-2-one, a disubstituted olefin, over both Lindlar catalyst and palladised barium sulphate (the two reactions are much slower in the presence of the former catalyst). Preparative hydrogenation of oct-7-en-5-yn-2-one over Lindlar catalyst, to an uptake of 2 mols. of hydrogen, gave a monoethylenic ketone, and comparison of its semicarbazone and 2 : 4-dinitrophenylhydrazone with authentic specimens showed that it was somewhat impure oct-*cis*-5-en-2-one.[8] The nature of the impurities was indicated by its infrared

[2] (*a*) Heilbron, Jones, and Sondheimer, *J.*, 1947, 1586; (*b*) Crombie, Harper, and Thompson, *J.*, 1951, 2906; (*c*) Crombie, *J.*, 1955, 1007; (*d*) Allan, Jones, and Whiting, *J.*, 1955, 1862; (*e*) Butenandt, Hecker, and Zachau, *Chem. Ber.*, 1955, **88**, 1185.
[3] Lebedev, Kobliansky, and Yakubchik, *J.*, 1925, **127**, 417.
[4] Dupont, *Bull. Soc. chim. France*, 1936, 1021, 1030.
[5] Crombie, Harper, Newman, Thompson, and Smith, *J.*, 1956, 126.
[6] Isler, Huber, Ronco, and Kofler, *Helv. Chim. Acta*, 1947, **30**, 1911.
[7] Lindlar, *ibid.*, 1952, **35**, 446.
[8] Harper and Smith, *J.*, 1955, 1512.

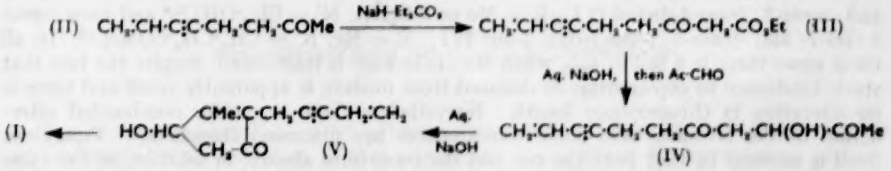
spectrum. Weak absorption at 910 and 995 cm.$^{-1}$ (unconjugated vinyl) suggested a little oct-7-en-2-one, and a weak band at 967 cm.$^{-1}$ (*trans*-CHR:CHR') suggested either oct-*trans*-6-en-2-one or oct-*trans*-5-en-2-one. Similar hydrogenation of hept-6-en-4-ynoic acid over Lindlar catalyst, to an uptake of 2 mols., gave a heptenoic acid and examination of its *p*-bromophenacyl ester showed it to be slightly impure hept-*cis*-4-enoic acid.[9]

Absorption of 2 mols. of hydrogen, over supported palladium catalysts, by the $\cdot CH_2 \cdot C{:}C \cdot CH{:}CH_2$ system thus proceeds mainly by selective reduction of the acetylenic to a *cis*-ethylenic linkage and by reduction of the terminal vinyl group. It remained to find out whether these processes are consecutive or concurrent.

Reduction of oct-7-en-5-yn-2-one over Lindlar catalyst, with interruption of the reaction when 1 mol. of hydrogen had been absorbed, gave products whose intensity of ultraviolet absorption (max. at 227 mμ; ε 9700—12,400) showed that the *cis*-diene ketone was present, though the infrared spectrum indicated that the hydrogenation had not been fully selective. On a larger scale, fractional distillation of the crude product gave material having max. at 227 mμ (ε 14,300—14,700). That this was substantially pure octa-*cis*-5 : 7-dien-2-one was confirmed by comparison of the infrared spectrum with that of authentic ketone prepared by the elimination of toluene-*p*-sulphonic acid from 8-toluene-*p*-sulphonyloxyoct-*cis*-5-en-2-one.[5] Mixed melting points of the semicarbazones and 2 : 4-dinitrophenylhydrazones showed no depressions. Similar hydrogenation of hept-6-en-4-ynoic acid gave substantially pure hepta-*cis*-4 : 6-dienoic acid, having max. at 226 mμ (ε 14,500). In the main, therefore, reduction of the acetylenic bond in vinylacetylenes takes place before that of the terminal vinyl group, as has been claimed by Zonis [10] and by Zal'kind and Khudekova.[11]

The way was then clear for the synthesis of *cis*-pyrethrolone, and, bearing in mind the greater stability of the pent-4-en-2-ynyl system over the *cis*-penta-2 : 4-dienyl system, we decided to make the selective hydrogenation the final stage.

Oct-7-en-5-yn-2-one (II) was converted, successively, by procedures previously devised,[12,13] into ethyl 2-oxo-oct-7-en-5-yne-1-carboxylate (III), its sodium salt, and 3-hydroxyundec-10-en-8-yne-2 : 5-dione (IV). The ultraviolet light absorption of these intermediates showed that the conjugated enyne system was unaffected by reagents used in the synthesis. Cyclisation then gave (±)-pent-4-en-2-ynylrethrolone (V), which readily formed a crystalline semicarbazone. That the product had the gross structure assigned to it was established by hydrogenation of the semicarbazone over palladised barium sulphate, with an uptake of 3 mols. of hydrogen, to the known tetrahydropyrethrolone semicarbazone.[14]




The ultraviolet light absorption of the hydroxy-ketone (max. at 226 mμ, ε 21,100) and its semicarbazone (max. at 227 and 267 mμ, ε 18,900 and 21,900) established the presence of a conjugated enyne chromophore. The latter was confirmed by the infrared spectrum of the hydroxy-ketone [conjugated disubstituted acetylene 2230 (m), conjugated vinyl 975 (s) and 925 (s), hydrogen-bonded hydroxyl 3410 (s), secondary hydroxyl 1052 (s), conjugated carbonyl stretching 1699 (s), conjugated ethylene 1652 (s) cm.$^{-1}$].

Catalytic hydrogenation of (±)-pent-4-en-2-ynylrethrolone over Lindlar catalyst to an uptake of 0·9 mol. of hydrogen gave the best specimen of (±)-*cis*-pyrethrolone (I), which

[9] Crombie and Harper, *J.*, 1952, 869.
[10] Zonis, *J. Gen. Chem.* (*U.S.S.R.*), 1939, **9**, 2191; *Chem. Abs.*, 1940, **34**, 4052.
[11] Zal'kind and Khudekova, *J. Gen. Chem.* (*U.S.S.R.*), 1940, **10**, 521; *Chem. Abs.*, 1940, **34**, 7847.
[12] Crombie, Edgar, Harper, Lowe, and Thompson, *J.*, 1950, 3552.
[13] Schechter, Green, and LaForge, *J. Amer. Chem. Soc.*, 1949, **71**, 3165; 1952, **74**, 4902.
[14] Crombie, Elliott, and Harper, *J.*, 1950, 971.

readily formed a crystalline semicarbazone. This product was identical with naturally derived pyrethrolone B-2[2b,15] (infrared spectrum and mixed m. p. of the semicarbazones).

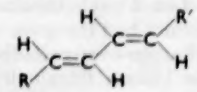
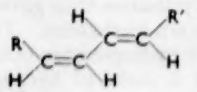
Ultraviolet-light absorptions of *cis*-pyrethrolone and precursors containing the *cis*-penta-2 : 4-dienyl system (Table) all have considerably lower intensities, owing to the diene chromophore, than their *trans*-counterparts: the wavelength of maximal absorption is similar in both stereoisomers. Small amounts of impurity in the *cis*-forms, resulting from

*Ultraviolet-light absorption of compounds containing the* cis- *and* trans-*penta*-2 : 4-*dienyl chromophore.*

| | *cis* | | | *trans* | | |
|---|---|---|---|---|---|---|
| | $\lambda_{max.}$ (mμ) | ε | Δε [a] | $\lambda_{max.}$ (mμ) | ε | Δε [a] |
| $CH_2$:CH·CH:CH·$CH_2$·OH | 227 | 14,300 | 14,300 | 226 | 25,200 | 25,200 |
| $CH_2$:CH·CH:CH·$CH_2$·$CO_2$H | 226 | 14,500 | 14,500 | — | — | — |
| $CH_2$:CH·CH:CH·$CH_2$·$CH_2$·CO·$CH_3$ | 226 | 16,100 | 16,100 [c] | 226 | 22,400 | 22,400 |
| | | | | (226 | 23,000 | 23,000) [b] |
| $CH_2$:CH·CH:CH·$CH_2$·$CH_2$·CO·$CH_2$·$CO_2$Et | — | — | — | 226 | 27,800 | 27,800 [b] |
| $CH_2$:CH·CH:CH·$CH_2$·$CH_2$·CO·$CH_2$·CH(OH)·CO·$CH_3$ | — | — | — | 226 | 22,600 | 22,600 |
| | | | | (226 | 27,500 | 27,500) [b] |
| Pyrethrolone (I) | 227 | 26,000 | 14,200 [c] | 227 | 37,400 | 25,600 [c] |
| | | | | (227 | 33,000 | 23,900) [b,d] |
| Semicarbazone of (I) | 228 | 18,300 | 14,000 [e] | 227 | 27,500 | 23,200 [e] |
| | 265 | 20,700 | — | 265 | 22,600 | — |

[a] Increase of ε at 227 mμ (*ca.* $\lambda_{max.}$) due to the $CH_2$:CH·CH:CH·$CH_3$ chromophore. [b] Part X. [c] Part VII. [d] Computed by deduction of $\varepsilon_{227}$ 11,800 for tetrahydropyrethrolone (max. at 230 mμ). [e] Computed by deduction of $\varepsilon_{227}$ 9100 for tetrahydropyrethrolone (max. at 227 mμ). [f] Computed by deduction of $\varepsilon_{227}$ 4300 for tetrahydropyrethrolone semicarbazone (max. at 264 mμ, ε 16,000).

the partial hydrogenation procedure, may be a contributory cause of the lower ε values but it is likely that the main cause is stereochemical. The system under consideration (VI; R = $CH_3$, R′ = H) is best compared with that of methyl deca-*trans*-2 : *cis*-4- and -*trans*-2 : *trans*-4-dienoate (VI; R = *n*-$C_5H_{11}$, R′ = $CO_2$Me),[2c] methyl *trans*-2 : *cis*-4- and

(VIa)   (VIb)

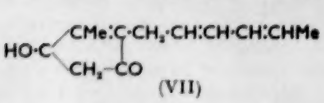
-*trans*-2 : *trans*-4-sorbate (VI; R = Me, R′ = $CO_2$Me),[2d] hexa- and deca-*trans*-2 : *cis*-4- and -*trans*-2 : *trans*-4-dienol (VI; R = Me or *n*-$C_5H_{11}$, R′ = $CH_2$·OH),[2c,e] and nona-*trans*-5 : *cis*-7- and -*trans*-5 : *trans*-7-dien-2-one (VI; R = Me, R′ = $CH_2$·$CH_2$·COMe).[16] In all these cases there is a fall in $\varepsilon_{max.}$ when the *cis*-linkage is introduced, despite the fact that steric hindrance to coplanarity, as deduced from models, is apparently small and there is no alteration in chromophore length. Nevertheless there is greater non-bonded interaction in the *cis*-forms and some consequences are discussed elsewhere.[2c] Piperylene itself is unusual in that both the *cis*- and the *trans*-form absorb, in solution, at the same wavelength and with equal intensity.[17] In the gas phase, however, *trans*- is reported to have a much higher $\varepsilon_{max.}$ than *cis*-piperylene.[18] Although *cis*-butadienylmethylcarbinol (hexa-*cis*-3 : 5-dien-2-ol)[17] and *cis*-1-phenylbutadiene[19] have lower $\varepsilon_{max.}$ values than their *trans*-counterparts, comparison with the system considered in this work is less valid as steric hindrance to coplanarity in the *cis*-forms is considerable: in *cis*-1-phenylbutadiene this is associated with a marked shift in the wavelength of maximal absorption (*cis*-, max. at 265—269 mμ, ε 18,400; *trans*-, max. at 280 mμ, ε 29,800).

For comparison with (±)-*cis*-pyrethrolone, preparation of (±)-*trans*-pyrethrolone was repeated by our earlier route,[2b] though the conditions were varied in an attempt to raise the overall yield. When 2 : 3-dichlorotetrahydropyran was treated with ethanolic ammonia

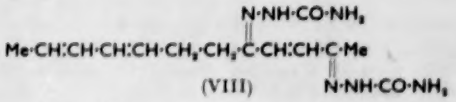
[15] West, *J.*, 1946, **463**.
[16] Crombie, Harper, and Smith, unpublished work.
[17] Braude and Coles, *J.*, 1951, 2085.
[18] Jacobs and Platt, *J. Chem. Phys.*, 1948, **16**, 1142.
[19] Grummitt and Christoph, *J. Amer. Chem. Soc.*, 1949, **71**, 4157.

and then, without isolation of the 3-chloro-2-ethoxytetrahydropyran, treated with potassium hydroxide, the yield of 2-ethoxy-5 : 6-dihydro-2-pyran obtained earlier [25] could not be reproduced, and a large proportion of 3-chloro-2-ethoxytetrahydropyran was recovered. Experiments showed that 3-chloro-2-ethoxytetrahydropyran eliminated hydrogen chloride much more rapidly with potassium hydroxide in hot diethylene glycol and this modification gave a consistent 40—45% yield of 2-ethoxy-5 : 6-dihydro-2-pyran. Since these experiments were completed Riobé has used ethylene glycol.[20] The use of 2 : 3-dibromotetrahydropyran was re-examined, and it was found that the decomposition which occurred on removal of the solvent (carbon tetrachloride) could be avoided by bromination in methylene chloride at −35° and removal of the solvent below 0° under reduced pressure. However, the yield of 2-ethoxy-5 : 6-dihydro-2-pyran was not improved. A crystalline semicarbazone was readily obtained from *trans*-octa-5 : 7-dien-2-one and this important intermediate was further characterised by ultraviolet and infrared absorption spectra. Improved yields were obtained at the ethoxycarbonylation stage by the use of the procedure of Schechter *et al.*[13] The final (±)-*trans*-pyrethrolone was obtained in enhanced purity, as judged by $\varepsilon_{max.}$ (37,400 against 33,000 found previously [25]), and by the ready formation of a crystalline semicarbazone (a semicarbazone was not obtained from our earlier preparation). This semicarbazone, although having the same m. p. as (±)-*cis*-pyrethrolone semicarbazone, gave a small but distinct depression of m. p. on admixture.

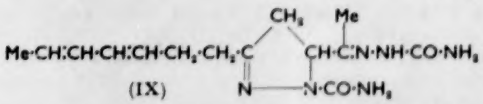
We have similarly prepared a diene analogue of pyrethrolone, sorbylrethrolone (VII), by successive conversion of sorbylacetone (nona-*trans*-5 : *trans*-7-dien-2-one *) into ethyl 2-oxonona-*trans*-5 : *trans*-7-diene-1-carboxylate, its sodium salt, and 3-hydroxydodeca-*trans*-8 : *trans*-10-diene-2 : 5-dione. The hydroxy-dione readily formed an " anhydrodisemicarbazone " which must be the disemicarbazone (VIII) of the triene-dione, rather than the pyrazoline (IX), for the ultraviolet absorption spectrum is consistent with the presence of a N:C·C:C·C:N system (max. at 315 mμ; ε 36,000). Similar " anhydrodisemicarbazones " have been obtained from 3-hydroxy-alkane- and -alkene-2 : 5-diones by Henze and Muller [21] and by Schechter, Green, and LaForge,[13] who considered, but did not exclude, the pyrazoline formulation. Cyclisation of the hydroxy-dione gave (±)-sorbylrethrolone, which formed a crystalline semicarbazone.




(VII)




(VIII)




(IX)

For insecticidal assay, (±)-*cis*-pyrethrolone was esterified with (+)-*trans*-chrysanthemic acid, through the acid chloride, to give a pyrethrin I [the mixed diastereoisomers (+)-*cis*-pyrethronyl (+)-*trans*-chrysanthemate and (−)-*cis*-pyrethronyl (+)-*trans*-chrysanthemate, the former of which is the naturally occurring ester]. (±)-Pent-4-en-2-ynylrethrolone was similarly esterified with (+)-*trans*-chrysanthemic acid, and (±)-sorbylrethrolone with (±)-*trans*-chrysanthemic acid. To avoid loss by thermal decomposition, none of these esters was purified by distillation, but all of them showed very high potency towards mustard beetle. Details of this and other insecticidal tests will be reported elsewhere.

## Experimental

Ultraviolet-light absorptions were determined for EtOH solutions by Mrs. I. Boston with a Hilger Medium Quartz Spectrograph. Some of the infrared-light absorptions were determined

* The preparation of all the stereoisomeric nona-5 : 7-dien-2-ones and a study of their spectral properties will be the subject of a future communication.

[20] Riobé, *Bull. Soc. chim. France*, 1952, 305.

[21] Henze and Muller, *Z. physiol. Chem.*, 1930, **193**, 88.

with a Grubb-Parsons single-beam spectrometer and others with a Grubb-Parsons double-beam spectrometer.

Benzene solutions of 2 : 4-dinitrophenylhydrazones were chromatographed on alumina before crystallisation from ethanol. M. p.s are corrected.

*Catalysts.*—5% Palladised calcium carbonate was prepared by the procedure of Busch and Stöve,[22] 5% palladised barium sulphate as given by Houben,[23] and lead-poisoned palladised calcium carbonate deactivated by quinoline by the procedure of Lindlar.[7] The Isler catalyst [6] (palladised charcoal deactivated by quinoline) was a gift from Dr. F. Sondheimer, whom we thank.

*Preparative Hydrogenation Procedure.*—Catalytic hydrogenations were conducted at room temperature and atmospheric pressure, generally in ethyl acetate. On completion or on interruption at the appropriate uptake, Filter-Cel was added. After filtration, the filtrate was washed (if quinoline had been added), with portions of 15% hydrochloric acid, then water, and dried ($MgSO_4$), and the product isolated by distillation.

*Hydrogenation of Oct-7-en-2-one and Oct*-trans-*5-en-2-one.*—Oct-7-en-2-one from our earlier preparation [9] gave a *semicarbazone*, crystallising as plates, m. p. 112·0—112·5°, from aqueous ethanol (Found: C, 59·0; H, 9·60. $C_9H_{17}ON_3$ requires C, 59·0; H, 9·35%). Regenerated from the semicarbazone by aqueous oxalic acid, oct-7-en-2-one had b. p. 66°/12 mm., $n_D^{20}$ 1·4306. The 2 : 4-dinitrophenylhydrazone had m. p. 65·0—65·5°. Catalytic hydrogenation of the semicarbazone gave octan-2-one semicarbazone, m. p. and mixed m. p. 124·5°. Catalytic hydrogenation of *oct*-trans-*5-en-2-one* [9] *semicarbazone*, m. p. 62·5—63·5° [from light petroleum (b. p. 60—80°)] (Found: C, 58·9; H, 9·25. $C_9H_{17}ON_3$ requires C, 59·0; H, 9·35%), similarly gave octan-2-one semicarbazone, m. p. and mixed m. p. 124°.

*Oct*-cis-*5-en-2-one.*—Oct-7-en-5-yn-2-one [8] (488 mg.), hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (100 mg.) in the presence of quinoline (35 mg.) to an uptake of 2 mols. (40 min.), gave impure oct-*cis*-5-en-2-one (350 mg.), b. p. 67—69°/17 mm., $n_D^{20}$ 1·4316. The semicarbazone (Found: C, 59·4; H, 9·4. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·35%) had m. p. 103·5—104·5°, raised on admixture with an authentic specimen [8] of m. p. 114°. The 2 : 4-dinitrophenylhydrazone (Found: C, 55·4; H, 6·05. Calc. for $C_{14}H_{18}O_4N_4$: C, 54·9; H, 5·9%) had m. p. 64°, raised on admixture with an authentic specimen [8] of m. p. 67·5°. In a similar experiment, but using quinoline (70 mg.), an uptake of 2 mols. of hydrogen was achieved in 4 hr.

*Octa*-cis-*5* : *7-dien-2-one.*—Oct-7-en-5-yn-2-one (2·38 g.) was hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (total, 1·0 g.) in the presence of quinoline (total, 1·0 g.) to an uptake of 1 mol. of hydrogen. The smaller amount of catalyst and quinoline first added was quickly deactivated and more was added to complete the hydrogenation. Fractional distillation gave octa-*cis*-*5* : 7-dien-2-one (0·91 g.), b. p. 62—67°/5 mm., $n_D^{20}$ 1·467—1·473, max. at 228 mμ (ε 15,000) (Found: C, 77·2; H, 9·55. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·75%). The *semicarbazone* (Found: C, 59·75; H, 8·5. $C_9H_{15}ON_3$ requires C, 59·65; H, 8·35%), crystallised thrice from aqueous ethanol, had m. p. 112·5—113·5°, raised to 112·5—114·0° on admixture with the derivative of m. p. 115·0—115·5° prepared by the elimination route.[5] The 2 : 4-*dinitrophenylhydrazone* (Found: C, 55·15; H, 5·2. $C_{14}H_{16}O_4N_4$ requires C, 55·2; H, 5·3%) had m. p. 55·0—55·5° and when admixed with the derivative of m. p. 52·5—53·5°, prepared by the elimination route,[5] had m. p. 53—54·5°.

*Hept*-cis-*4*-*enoic Acid.*—Hept-6-en-4-ynoic acid (622 mg.),[8] hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (500 mg.) in the presence of quinoline (1·1 g.) to an uptake of 2 mols. (10 min.), gave slightly impure hept-*cis*-4-enoic acid (500 mg.), b. p. 116·0—116·5°/12 mm., $n_D^{20}$ 1·4426. The *p*-bromophenacyl ester, crystallised from aqueous ethanol, had m. p. 41—42° raised to 41—42·5° on admixture with the authentic ester [9] of m. p. 44°. Crombie and Harper [9] record b. p. 116°/12 mm., $n_D^{20}$ 1·4400, for hept-*cis*-4-enoic acid.

*Hepta*-cis-*4* : *6-dienoic Acid.*—Hept-6-en-4-ynoic acid (621 mg.), hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (300 mg.) in the presence of excess of quinoline (1·1 g.) to an uptake of 1 mol. of hydrogen (15 min.), gave *hepta*-cis-*4* : *6-dienoic acid* (240 mg.), b. p. 122—124°/12 mm., $n_D^{20}$ 1·4749 (for light absorption see Table) (Found: C, 67·0; H, 8·1. $C_7H_{10}O_2$ requires C, 66·7; H, 8·0%). The p-*bromophenacyl ester* was formed readily and crystallised as plates (from aqueous ethanol), m. p. 80—81° (Found: C, 56·0; H, 4·6. $C_{15}H_{15}O_3Br$ requires C, 55·7; H, 4·7%).

[22] Busch and Stöve, *Ber.*, 1916, **49**, 1063.
[23] Houben, "Die Methoden der Organische Chemie," Thieme, Leipzig, Vol. II, p. 500.

*Ethyl 2-Oxo-oct-7-en-5-yne-1-carboxylate.*—By the procedure of Part V,[12] on a 0·05—0·20-molar scale, oct-7-en-5-yn-2-one was treated with sodium hydride in ethyl carbonate–ether, to give *ethyl 2-oxo-oct-7-en-5-yne-1-carboxylate* (44—46%), b. p. 77—85°/0·1 mm., 88—98°/0·3 mm., $n_D^{20}$ 1·478—1·483, max. at 223 and 228 mμ (ε 14,000 and 11,600) (Found: C, 67·75; H, 7·25. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·25%). The consistent b. p. spread might be due to partial separation of keto- and enol forms or to some methylene-*C* substitution.

*3-Hydroxyundec-10-en-8-yne-2 : 5-dione.*—By a procedure similar to that of Part V,[12] ethyl 2-oxo-oct-7-en-5-yne-1-carboxylate (11·1 g.) was shaken under nitrogen with 3% aqueous sodium hydroxide (85 ml.) during 6 hr. at 20° and then set aside overnight at 0°. A little insoluble oil was removed by light petroleum and recovered by distillation (b. p. 80—90°/12 mm., $n_D^{20}$ 1·476; 0·3 g.). It was identified as oct-7-en-5-yn-2-one, presumably formed by ketonic hydrolysis, by conversion into the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 67—68°.

68% w/v Aqueous pyruvaldehyde (7·3 ml.) was added to the clear alkaline solution and the pH adjusted to 8·5. The mixture was kept at 35°, separation of oil starting after 20 min. When this appeared complete (*ca.* 5 ml.) sodium chloride was added and the product isolated with ether. Drying ($Na_2SO_4$) and distillation gave *3-hydroxyundec-10-en-8-yne-2 : 5-dione* (4·61 g., 42%), b. p. 115—117°/0·1 mm., $n_D^{20}$ 1·5035, max. at 223 and 232 mμ (ε 13,600 and 8900) (Found: C, 67·7; H, 7·35. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·25%).

The aqueous layer was acidified with concentrated hydrochloric acid (an oil separated) and warmed to 50°, but little decarboxylation occurred. Extraction with ether, drying ($Na_2SO_4$), and distillation (b. p. 60—90°/0·4 mm.) gave a crystalline product (0·15 g.), which after crystallisation from light petroleum (b. p. 40—60°) was identified as hept-6-en-4-ynoic acid by m. p. and mixed m. p. 57—58·5°. In addition, some polymeric material was obtained but no hydroxy-dione was present in this extract (contrast Part V [12]).

*(±)-Pent-4-en-2-ynylrethrolone* [*(±)-4-Hydroxy-3-methyl-2-(pent-4-en-2-ynyl)cyclopent-2-en-1-one*].—3-Hydroxyundec-10-en-8-yne-2 : 5-dione (8·6 g.) was added during 1 hr. to 2% sodium hydroxide solution (125 ml.) containing a trace of quinol and stirred at 10°. After a further hour's stirring at room temperature, sodium chloride was added and the product isolated with ether. Distillation gave *(±)-pent-4-en-2-ynylrethrolone* (3·27 g., 42%), b. p. 128—131°/0·1 mm., $n_D^{20}$ 1·5520, light-absorption max. in Table (Found: C, 74·8; H, 6·95. $C_{11}H_{12}O_2$ requires C, 74·95; H, 6·85%). Stored at 0° in the presence of quinol and under nitrogen, the hydroxy-ketone did not deteriorate during several months.

The *semicarbazone* was formed readily with semicarbazide hydrochloride in pyridine and crystallised from ethanol as needles, light-absorption max. in Table (Found: C, 61·8; H, 6·6. $C_{12}H_{15}O_2N_3$ requires C, 61·8; H, 6·5%). When heated, the semicarbazone blackened and sintered without a definite m. p. or decomposition temperature. Catalytic hydrogenation of the semicarbazone over palladised barium sulphate, with an uptake of 3 mols. of hydrogen, gave tetrahydropyrethrolone semicarbazone, m. p. and mixed m. p. 174—175°.

*(±)-cis-Pyrethrolone* [*(±)-4-Hydroxy-3-methyl-2-(penta-cis-2 : 4-dienyl)cyclopent-2-en-1-one*]. (±)-Pent-4-en-2-ynylrethrolone (500 mg.), hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) catalyst (100 mg.) in the presence of quinoline (250 mg.) to an uptake of 0·9 mol. of hydrogen, gave (±)-cis-*pyrethrolone* (200 mg.), b. p. 120—123°/0·06 mm., $n_D^{20}$ 1·536, light absorption see Table (Found: C, 73·9; H, 7·95. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·9%).

In another reduction, over 200 mg. of catalyst with 200 mg. of quinoline, the uptake was very rapid and the product, max. at 227 mμ (ε 21,800) (Found: C, 73·6; H, 8·2%), contained some overhydrogenated material. The *semicarbazone* prepared from this by the semicarbazide hydrochloride–pyridine method and crystallised from ethanol had m. p. 198·5—200° (decomp.) (immersed at 195°; rise in temp. 5° per min.) (for light absorption see Table) (Found: C, 61·1; H, 7·4. $C_{12}H_{17}O_2N_3$ requires C, 61·2; H, 7·3%). Admixed with pyrethrolone B-2 semicarbazone [m. p. 205—206° (decomp.)], the m. p. was raised to 201—203° (decomp.) (immersed at 195°). On admixture with (±)-*trans*-pyrethrolone semicarbazone [m. p. 199—200° (decomp.)], the m. p. was lowered to 194—195° (decomp.) (immersed at 190°).

*(±)-Tetrahydropyrethrolone* [*(±)-4-Hydroxy-3-methyl-2-pentylcyclopent-2-en-1-one*].—By the procedure used above for (±)-pent-4-en-2-ynylrethrolone, ethyl 2-oxo-octane-1-carboxylate (44 g.) was converted into 3-hydroxyundecane-2 : 5-dione and, without distillation, this was cyclised to (±)-tetrahydropyrethrolone (12·6 g., 32% overall), b. p. 134—137°/0·4 mm., $n_D^{20}$

[24] Quennehen and Normant, *Compt. rend.*, 1949, **228**, 1301.
[25] Woods and Sanders, *J. Amer. Chem. Soc.*, 1946, **68**, 2483.

1·4901, max. at 230 mμ (ε 11,800) (Found : C, 72·1; H, 10·0. Calc. for $C_{11}H_{18}O_3$ : C, 72·5; H, 10·0%). Prepared with semicarbazide hydrochloride in pyridine and crystallised from ethyl acetate, the semicarbazone formed prisms, m. p. 175·5—177°, max. at 264 mμ (ε 16,000; $\varepsilon_{237}$ *ca.* 4300) (Found : C, 60·5; H, 8·85. Calc. for $C_{12}H_{21}O_3N_3$ : C, 60·2; H, 8·85%). By use of commercial aqueous pyruvaldehyde a yield of 9% (overall) of (±)-tetrahydropyrethrolone having max. at 227 mμ (ε 9100) was obtained previously.[25]

*2-Ethoxy-5 : 6-dihydro-2-pyran.*—Material from 2 : 3-dichlorotetrahydropyran,[25] insoluble in aqueous phosphoric acid, was washed with sodium carbonate solution, dried, and fractionally distilled. The largest fraction, b. p. 73·0—73·5°/14 mm., $n_D^{20}$ 1·4565 (Found : C, 50·3; H, 7·7; Cl, 24·9; OEt, 23·2. Calc. for $C_7H_{13}O_2Cl$ : C, 51·0; H, 7·95; Cl, 21·6; OEt, 27·3%), was mainly 3-chloro-2-ethoxytetrahydropyran. Quennehen and Normant[24] record b. p. 73—74°/13 mm., for 3-chloro-2-ethoxytetrahydropyran prepared by the action of sodium ethoxide on 2 : 3-dichlorotetrahydropyran.

Potassium hydroxide (100 g.) was added to crude 3-chloro-2-ethoxytetrahydropyran (150 g.) in diethylene glycol (400 ml.), and the mixture stirred at 160—170° under reflux for 2 hr. The product was isolated by distillation under reduced pressure. Redistillation gave 2-ethoxy-5 : 6-dihydro-2-pyran[25] (46·5 g., 40%), b. p. 50—52°/13 mm., $n_D^{20}$ 1·443—1·446.

*Octa*-trans-5 : 7-*dien*-2-*one*.—The ketone formed a *semicarbazone*, crystallising from aqueous ethanol as plates, m. p. 96·5—98° (Found : C, 59·9; H, 8·55. $C_9H_{15}ON_3$ requires C, 59·65; H, 8·35%).

(±)-trans-*Pyrethrolone* [(±)-4-*Hydroxy*-3-*methyl*-2-(*penta*-trans-2 : 4-*dienyl*)cyclo*pent*-2-*en*-1-*one*].—By the procedure used above for (±)-pent-4-en-2-ynylrethrolone, ethyl 2-oxo-octa-*trans*-5 : 7-diene-1-carboxylate (13·1 g.) was converted into 3-hydroxyundeca-*trans*-8 : 10-diene-2 : 5-dione (4·8 g., 37%), b. p. 112—113°/0·1 mm., $n_D^{20}$ 1·5000. No hydroxy-dione was obtained on acidification of the extracted aqueous layer. Cyclisation then gave (±)-*trans*-pyrethrolone (52%), b. p. 132—134°/0·15 mm., $n_D^{20}$ 1·5447. For light absorption see Table. A *semicarbazone* was formed readily in semicarbazide hydrochloride–pyridine and, crystallised from ethanol, had m. p. 199—200° (decomp.) (Found : C, 61·3; H, 7·3. $C_{13}H_{17}O_3N_3$ requires C, 61·25; H, 7·3%). Catalytic hydrogenation of the semicarbazone over palladised barium sulphate, with an uptake of 2 mols. of hydrogen, gave (±)-tetrahydropyrethrolone semicarbazone, m. p. and mixed m. p. 175—176°.

*Ethyl* 2-*Oxonona*-trans-5 : trans-7-*diene*-1-*carboxylate*.—By the procedure of Part V,[12] nona-*trans*-5 : *trans*-7-dien-2-one (22·1 g.) was ethoxycarbonylated, to *ethyl* 2-*oxonona*-trans-5 : trans-7-*diene*-1-*carboxylate* (14·3 g., 43%), b. p. 89—99°/0·2 mm., $n_D^{20}$ 1·478—1·484, max. 228 mμ (ε 25,200) (Found : C, 68·9; H, 8·55. $C_{13}H_{18}O_3$ requires C, 68·6; H, 8·65%).

3-*Hydroxydodeca*-trans-8 : trans-10-*diene*-2 : 5-*dione*.—By procedure A of Part V,[12] ethyl 2-oxonona-*trans*-5 : *trans*-7-diene-1-carboxylate (6·0 g.) was hydrolysed and treated with 68% aqueous pyruvaldehyde, to give 3-*hydroxydodeca*-trans-8 : trans-10-*diene*-2 : 5-*dione* (3·23 g., 54%), b. p. 126—133°/0·4 mm., $n_D^{20}$ 1·498—1·502, max. at 227 mμ (ε 26,600) (Found : C, 68·7; H, 8·65. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·65%).

By the procedure of Schechter *et al.*[13] the hydroxy-dione gave an immediate precipitate with semicarbazide hydrochloride in pyridine–ethanol. On crystallisation from ethanol the yellow sparingly soluble "*anhydrodisemicarbazone*" (*dodeca*-trans-3 : trans-8 : trans-10-*triene*-2 : 5-*dione disemicarbazone*) had m. p. 224—227° (decomp.), max. at 227 and 315 mμ (ε 24,000 and 36,000) (Found : C, 54·75; H, 7·0. $C_{14}H_{22}O_3N_6$ requires C, 54·85; H, 7·25. Calc. for the disemicarbazone, $C_{14}H_{24}O_3N_6$ : C, 51·85; H, 7·45%).

(±)-*Sorbylrethrolone* [(±)-2-(*Hexa*-trans-2 : trans-4-*dienyl*)-4-*hydroxy*-3-*methyl*cyclo*pent*-2-*en*-1-*one*].—By the procedure of Part V,[12] 3-hydroxydodeca-*trans*-8 : *trans*-10-diene-2 : 5-dione (2·9 g.) was cyclised to (±)-*sorbylrethrolone* (0·80 g., 30%), b. p. 130—138°/0·2 mm., $n_D^{20}$ 1·539, max. at 227 mμ (ε 30,000) (Found : C, 74·9; H, 8·5. $C_{12}H_{16}O_3$ requires C, 74·95; H, 8·4%). The reason for the comparatively low ε value is uncertain. The *semicarbazone* prepared with semicarbazide hydrochloride in pyridine–ethanol and crystallised from ethanol had m. p. 210—212° (decomp.) (Found : C, 62·45; H, 7·6. $C_{13}H_{19}O_3N_3$ requires C, 62·6; H, 7·65%). No maleic anhydride adduct could be obtained from sorbylrethrolone.

*Chrysanthemic Esters.*—By the procedure of Part V,[12] interaction of (±)-pent-4-en-2-ynylrethrolone (508 mg.) and (+)-*trans*-chrysanthemoyl chloride (573 mg.) in pyridine–benzene, and heating the product at 0·05 mm./60° for 1 hr., gave (±)-*pent*-4-*en*-2-*ynylrethronyl* (+)-trans-*chrysanthemate* (780 mg.), $n_D^{20}$ 1·523, max. at 225 mμ (ε 29,000) (Found : C, 77·35; H, 8·35. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·05%).

In a similar way, interaction of (±)-*cis*-pyrethrolone (114 mg.) and (+)-*trans*-chrysanthemoyl

chloride (133 mg.) gave (±)-*cis-pyrethronyl* (+)-trans-*chrysanthemate* (205 mg.), $n_D^{20}$ 1·514, max. at 225 mμ (ε 28,900) (Found: C, 75·4; H, 8·7. $C_{21}H_{28}O_3$ requires C, 76·8; H, 8·6%).

Interaction of (±)-sorbylrethrolone (500 mg.) and (±)-*trans*-chrysanthemoyl chloride (535 mg.) gave (±)-*sorbylrethronyl* (±)-trans-*chrysanthemate*, $n_D^{20}$ 1·517, max. at 226 mμ (ε 38,300) (Found: C, 77·1; H, 9·0. $C_{22}H_{30}O_3$ requires C, 77·15; H, 8·85%).

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## 773. *Oxidation by Nitrous and Nitric Acid. Part IV.* Spectroscopic Investigation of the Equilibrium between* $NO^+$ *and Nitrous Acid in Aqueous Perchloric Acid.*

By K. SINGER and (MISS) P. A. VAMPLEW.

The disappearance of the absorption spectrum of molecular nitrous acid (weak maxima between λ 3400 and 3900 Å) and the appearance of a strong absorption band ($\varepsilon_{max.} \approx 4200$ at 2600 Å), attributed to $NO^+$, are perceptible in 45% and complete in 58% (w/w) perchloric acid. Spectrophotometric measurements show that molecular nitrous acid and $NO^+$ account, within the limits of error (±5%), for the total "analytical" nitrous acid in 1—68% aqueous perchloric acid.

RAMAN lines attributed to $NO^+$ have been observed by Angus and Leckie [1] in aqueous perchloric acid; the lines were intense in 62%, weak in 48%, and absent in 40% perchloric acid. These Raman lines are also found in solutions of dinitrogen trioxide in sulphuric acid media.[2] A recent note by Bayliss and Watts [3] reported the disappearance of the ultraviolet absorption spectrum of nitrous acid and the concurrent appearance of a broad band ($\lambda \approx 2500$ Å; $\varepsilon \approx 3900$) in aqueous sulphuric acid. These authors attribute this band to $NO^+$; they plot (without giving details of their method) the composition of their media with respect to molecular nitrous acid and $NO^+$ against percentage of sulphuric acid and they conclude, from the fact that the two entities do not account for the total, that an appreciable fraction of nitrous acid is converted into a third entity (such as $H_2NO_2^+$) in some of the media.

Preliminary experiments (carried out before the work of Bayliss and Watts had come to our notice) showed that increase in acidity caused similar changes in the absorption spectrum of nitrous acid in aqueous sulphuric and in aqueous perchloric acid. While, however, the positions of the absorption maxima are almost unaffected by change of acidity in aqueous perchloric acid, a marked effect due to the medium is observed in aqueous sulphuric acid; thus the maximum of the broad band attributed to $NO^+$ moves from $\lambda \approx 2550$ Å to 2300 Å in 60—90% sulphuric acid, and in the more aqueous media appreciable displacements also occur in the region of the maxima of nitrous acid. This feature makes spectrophotometric analysis of the absorption spectra in sulphuric acid media almost impossible. A major experimental difficulty in sulphuric as well as in perchloric acid media arises from the volatility of nitrous acid (except at acidities sufficiently high to convert nitrous acid completely into $NO^+$). Although the use of closed optical cells effectively prevents appreciable loss of nitrous acid during optical measurements, the concentration of "analytical" nitrous acid (*i.e.*, all entities which diazotise aromatic

* Part III, *J.*, 1956, 1143.

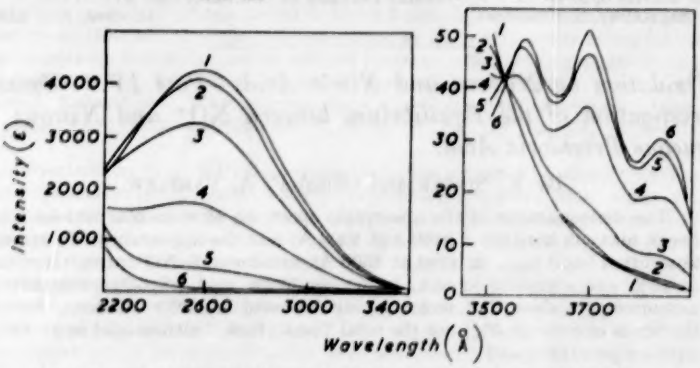
[1] Angus and Leckie, *Proc. Roy. Soc.*, 1935, *A*, **150**, 615.
[2] Millen, *J.*, 1950, 2600.
[3] Bayliss and Watts, *Chem. and Ind.*, 1955, 1353.

amines under the conditions of the colorimetric method of analysis used) decreases by 5—10% in the short time between two consecutive withdrawals (by pipette) of samples for analysis from the solutions prepared for spectroscopic measurements. The resultant errors in the determination of the extinction curves were appreciably reduced by a procedure described in the Experimental section.

## Summary and discussion of the results

The ultraviolet absorption spectra of nitrous acid in 40—60% perchloric acid media are shown in Figs. 1(*a*) and (*b*); extinction coefficients at λ 2600, 3700, 3840, and 3520 Å

Fig. 1*a*. Fig. 1*b*.




1, 58%; 2, 55·6%; 3, 53·0%; 4, 50·4%; 5, 47·9%; 6, 41% $HClO_4$.

are listed in the Table. The characteristic bands of molecular nitrous acid (maxima at λ 3700, 3560, and 3840 Å) begin to weaken in approx. 45% perchloric acid and have completely vanished in 58% perchloric acid. The disappearance of these weak maxima is accompanied by the appearance of a broad band (λ ≈ 2600 Å) which reaches its maximum

| | | | | | $100 \times [NO^+]/(HNO_2)$ calculated from | | |
|---|---|---|---|---|---|---|---|
| $HClO_4$ (% w/w) | $\varepsilon_{2600}$ 1 | $\varepsilon_{3700}$ 2 | $\varepsilon_{3840}$ 3 | $\varepsilon_{3520}$ | $\varepsilon_{2600}$ | $\varepsilon_{3700}$ | $\varepsilon_{3840}$ |
| 60·5 | 4230 | 9·1 | 2·1 | 46·1 | 100 | 100 | 100 |
| 58·0 | *4240* | *9·3* | *2·1* | 45·0 | *100* | *100* | *100* |
| 55·6 | 4040 | 10·6 | 3·5 | 43·9 | 95·3 | 96·8 | 95·1 |
| 53·0 | 3200 | 17·2 | 7·7 | 42·7 | 75·5 | 81·2 | 80·3 |
| 50·4 | 1650 | 36·2 | 19·0 | 41·6 | 38·8 | 36·2 | 40·5 |
| 47·9 | 447 | 46·5 | 27·3 | 40·6 | 10·2 | 11·6 | 11·3 |
| 45·0 | 130 | 50·3 | 30·0 | 39·6 | 2·73 | 2·61 | 1·76 |
| 41·9 | 46·0 | 50·6 | 30·4 | 38·6 | 0·73 | (0·19) | (0·036) |
| 38·5 | 25·1 | *51·4* | *30·5* | 37·5 | 0·24 | *0* | *0* |
| 35·5 | 17·0 | 50·7 | 30·2 | 36·5 | 0·052 | — | — |
| 31·5 | 13·9 | 50·4 | 29·6 | 35·5 | (−0·021) | — | — |
| 27·5 | 14·8 | 49·7 | 29·3 | 34·5 | *0* | — | — |

Values assumed to correspond to 100% and 0% of $NO^+$ are italicised. Calculated values which are considered as not significant are in parentheses.

intensity (ε 4240) when the spectrum of molecular nitrous acid has completely disappeared. Further features, not evident from the Table and Figs. 1(*a*) and (*b*) are: the position and intensity of the maximum at 2600 Å do not change appreciably in 58—68% perchloric acid (though the extinction curve drops more steeply between 2600 and 2200 Å as acidity increases); the highest peak of molecular nitrous acid ($\lambda_{max.}$ 3700, ε 51·4) does not alter in intensity, and moves gradually towards $\lambda_{max.}$ 3720 Å as the acidity is reduced below 40% perchloric acid.

The assignment of the broad band at 2600 Å to $NO^+$, first made by Bayliss and Watts,[3] can be justified by the following arguments: (1) the stability of the nitrous acid solution in concentrated (*i.e.*, >58%) perchloric acid indicates that an ionic entity has been formed; (2) the validity of Beer's law shows that a molecule of this entity is formed from one molecule of nitrous acid; (3) the similarity of the absorption spectra in perchloric and sulphuric acid media indicates that the same entity is formed in both acids; (4) if the entity were $H_2NO_2^+$, one would not expect the spectrum to be almost unchanged in 58—68% perchloric acid, or to persist with undiminished intensity (although shifted towards shorter wavelengths) in up to 90% sulphuric acid.

The fraction of " analytical " nitrous acid converted into $NO^+$ in $p$% perchloric acid was calculated from $\varepsilon_{2600}(=\varepsilon_1)$ on the assumption that the spectra in 58% and 27·5% acid are,

FIG. 2.

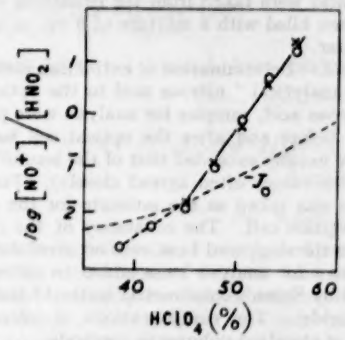
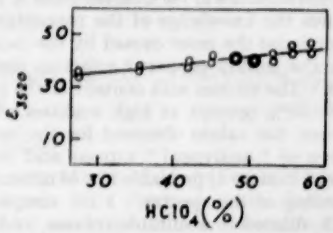



FIG. 3.




○ *Calc. from* $\varepsilon_{2600}$.
× *Calc. from the mean between* $\varepsilon_{3700}$ *and* $\varepsilon_{3840}$.

respectively, those of $NO^+$ and molecular nitrous acid: $[NO^+]/(HNO_2) = [\varepsilon_1(p\%) - \varepsilon_1(27{\cdot}5\%)]/[\varepsilon_1(58\%) - \varepsilon_1(27{\cdot}5\%)]$, where $(HNO_2)$ denotes the concentration of " analytical " nitrous acid.

The fraction of molecular nitrous acid converted into other entities was similarly obtained from $\varepsilon_{3700}(=\varepsilon_2)$ and $\varepsilon_{3840}(=\varepsilon_3)$:

$$\{(HNO_2) - [HNO_2]\}/(HNO_2) = [\varepsilon_2(38{\cdot}5\%) - \varepsilon_2(p\%)]/[\varepsilon_2(38{\cdot}5\%) - \varepsilon_2(58\%)]$$

and similarly for $\varepsilon_3$.

The calculations were based on $\varepsilon$ values in 58% and 38·5% rather than 27·5% perchloric acid because of a slight displacement of the maxima from 3700 and 3840 Å between 38·5% and 27·5% perchloric acid. The results listed in the last three columns of the Table show that the concentration of $NO^+$ agrees within the limits of error with the decrease in concentration of molecular nitrous acid. These figures and the appearance of the spectra give no indication of the presence of a third entity such as $H_2NO_2^+$, but they do not exclude the possibility that up to approx. 5% of the " analytical " nitrous acid is converted into a third entity in some of the perchloric acid media.

When the logarithm of the ratio $[NO^+]/[HNO_2]$ ($[HNO_2]$ being the concentration of molecular nitrous acid) calculated from the entries in the Table, is plotted against percentage of perchloric acid, the points lie close to a straight line (Fig. 2) (except at low acidities). One would expect the slope of this line to be similar to that of the $-J_0$ function which governs the dissociation equilibrium for certain indicators in which proton uptake is accompanied by elimination of water. The slope of log ($[NO^+]/[HNO_2]$), however, exceeds that of the $-J_0$ function for perchloric[4,5] acid by a factor of 2·7 (Fig. 2). This surprising feature must be attributed to a strong dependence of the activity coefficients of molecular nitrous

[4] Hammet and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2734.
[5] Robinson and Baker, *Trans. Proc. Roy. Soc. N Z.*, 1946, **76**, 250.

acid, and perhaps of $NO^+$, on the composition of the medium. This is qualitatively supported by two observations: (*a*) addition of sodium perchlorate has a similar (though weaker) effect on the equilibrium as increase of acidity; (*b*) the instability of nitrous acid solutions of a given concentration increases markedly in 35—50% perchloric acid: this must be ascribed to a corresponding increase of the partial pressure (and hence of the activity coefficient) of molecular nitrous acid.

## Experimental

*Materials.*—" AnalaR " perchloric acid (72%) and sodium nitrite were used.

*Preparation of solutions.* 9 ml. of ice-cooled aqueous perchloric acid of the appropriate strength were added to 1 ml. of aqueous sodium nitrite of the required concentration ($10^{-3}$M to $b \times 10^{-3}$M). The optical cell was flushed and then filled with part of this solution; samples for determination of the concentration of nitrous acid were taken from the remaining solution (see below). The reference cell was flushed and then filled with a mixture of 9 ml. of aqueous perchloric acid of the same strength and 1 ml. of water.

*Determination of the Concentration of Nitrous Acid.*—Determination of extinction coefficients requires the knowledge of the concentration of " analytical " nitrous acid in the optical cell. To minimise the error caused by the escape of nitrous acid, samples for analysis were pipetted from the freshly prepared solutions immediately before and after the optical cell had been filled. The nitrous acid content of the first sample usually exceeded that of the second sample by 5—10% (except at high acidities when the two values often agreed closely). The mean between the values obtained for the two samples was taken as the estimate for the concentration of " analytical " nitrous acid in the absorption cell. The constancy of the readings showed that no appreciable loss of nitrous acid from the stoppered 1 cm. cells occurred during the recording of the spectra. 1 ml. samples withdrawn for analysis were added to an excess of alkali, diluted to a suitable volume, and measured by Shinn's colorimetric method [6] (sulphanilamide + *N*-naphthylethylenediamine dihydrochloride). The concentrations of nitrous acid were too low ($10^{-4}$ to $5 \times 10^{-3}$M) to permit the use of standard volumetric methods.

*Determination of the Extinction Curves.*—The spectra were measured on a Hilger " Uvispek " spectrophotometer. The optical cells were kept thermostatically at 25° ± 0·3°. As solutions of different nitrous acid concentrations had to be employed for different parts of the spectrum, and as the error in the estimation of nitrous acid in any given solution was considered to be too high (probably more than ±5%), the following procedure was adopted: in all the media investigated the ratios of the extinction at all wavelengths ($\varepsilon_\lambda$) to the extinction at 3520 Å were determined; previous experiments had shown that $\varepsilon_{3520}$ varied but slowly with acidity. This involved no errors of analysis (although the validity of Beer's law is assumed). For each medium $\varepsilon_{3520}$ was then determined repeatedly by the method described above, and the values of $\varepsilon_{3520}$ were plotted against % perchloric acid. The ordinates of the " best " straight line drawn through these points (Fig. 3) were regarded as the most reliable estimates for $\varepsilon_{3520}$. Extinction coefficients at other wavelengths were then calculated from the ratios of $\varepsilon_\lambda/\varepsilon_{3520}$. Although this procedure greatly improved reproducibility, substantially similar results for ratios $[NO^+]/(HNO_2)$ and $\{(HNO_2) - [HNO_2]\}/(HNO_2)$ were obtained when the extinction curves were determined by the usual method.

*Evaluation of the Extinction Curves.*—Calculations of composition were based on the extinction coefficients at 2600, 3700, and 3840 Å. 2600 Å is an obvious choice because the extinction curve at high acidities has a flat maximum of $\varepsilon$ 4240 while $\varepsilon$ at low acidities is only 15. 3700 Å is the position of the highest peak of molecular nitrous acid in the relevant range of acidities with $\varepsilon$ 51·4, while at high acidity $\varepsilon$ = 9·3. The difference between the extinction at low and high acidities at other wavelengths in the range of the bands of molecular nitrous acid is smaller; results calculated by means of the values of $\varepsilon$ at 3840 Å, the position of another peak of molecular nitrous acid ($\varepsilon$ 30·5 and 2·1 at low and high acidity, respectively), agree fairly well with those calculated from $\varepsilon_{3700}$ (Table).

We thank Mrs. J. Briggs for assisting in the experimental work, the Council of Royal Holloway College for a studentship, the Ministry of Education for a maintenance grant (to P. A. V.), and Imperial Chemical Industries Limited for financial assistance.

Royal Holloway College, Englefield Green. [*Received, June 4th*, 1956.]

[6] Shinn, *Ind. Eng. Chem. Anal.*, 1941, **13**, 33; Kershaw and Chamberlin, *ibid.*, 1942, **14**, 312.

## 774. 7-(2 : 3-*Dihydroxypropyl*)*theophylline.*

By David B. Ishay.

This substance [1] is best prepared as follows :

Theophylline (180 g.; dehydrated) is dissolved in N-potassium hydroxide, the solution evaporated to dryness on a water-bath, and the residual potassium salt dried *in vacuo*. It is added portionwise, with stirring, to α-chlorohydrin (122 g.) at 115° during 40—60 min. The mixture is then heated at 120—125° for 1 hr., and methanol (500 c.c.) is dropped in with stirring. The precipitated potassium chloride is filtered off and washed with methanol (50 c.c.). Cooling the filtrate and washings in ice–salt causes crystallisation of 7-(2 : 3-dihydroxypropyl)theophylline which was washed with acetone–methanol (1 : 1; 2 × 50 c.c.). The product (198 g., 78%) then has m. p. 155—158°.

Hillel Remedy Factory Ltd.,
Haifa Bay, Israel.

[*Received, February 2nd,* 1956.]

[1] Maney, Jones, and Korns, *J. Amer. Pharm. Assoc.*, 1946, **35**, 266; U.S.P. 2,575,344.

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## 775. *Effect of Added Hydroxy-compounds on the Association of Benzoic Acid.*

By Winifred G. Wright.

Previously it had been shown [1] that very small concentrations of water in benzene increase the association of benzoic acid in that solvent. The three alcohols, di-*p*-*tert*.-butylphenyl- and di-*p*-methoxyphenyl-methanol and 1-β-naphthylethanol, have now been found to exert a similar effect, the increase in association produced by the alcohol being comparable to that obtained by a similar concentration of water and becoming greater with increase of alcohol concentration.

The experimental methods were as described previously.[1] Plots of degree of association against concentration of solute at constant concentration of alcohol had the same shape as that recorded earlier for the association of benzoic acid in benzene in the presence of water and tended to become parallel to the concentration axis; rounded values of $M/M_0$ at 0·10 mole of solute/1000 g. of solvent are recorded in the Table.

| Solute | Concn. of added alcohol (moles/1000 g. of solvent) | $M/M_0$ |
|---|---|---|
| Nil | — | 1·6 |
| Water | 0·0158 | 1·9 |
| Di-*p*-*tert*.-butylphenylmethanol | 0·0155 | 1·9 |
| Di-*p*-methoxyphenylmethanol | 0·0158 | 1·9 |
| 1-β-Naphthylethanol | 0·0139 | 1·8 |
| „ „ | 0·0239 | 1·9 |

University of Natal, Durban.

[*Received, March 27th,* 1956.]

[1] Wright, *J.*, 1949, 683.

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## 776. *The Preparation of* [2 : 4 : 7 : 9-$^{14}C_1$]-1 : 10-*Phenanthroline and* [4 : 4′ : 6 : 6′-$^{14}C_1$]-2 : 2′-*Dipyridyl.*

By Peter Ellis, R. G. Wilkins, and M. J. G. Williams.

In continuation of our studies [1] of exchange reactions of complex ions by using labelled ligands we have synthesized [$^{14}$C]-1 : 10-phenanthroline in yields better than those of reported preparations [2,3] of the inactive material.

[1] Popplewell and Wilkins, *J.*, 1955, 4098.
[2] Halcrow and Kermack, *J.*, 1946, 155.
[3] Breckenridge and Singer, *Canad. J. Res.*, 1947, **25**, *B*, 583.

1 : 10-Phenanthroline is usually prepared by a Skraup reaction [4] between *o*-phenylenediamine and glycerol in the presence of sulphuric and arsenic acids. Carbon-14 can therefore be introduced into the phenanthroline molecule *via* either (*a*) labelled diamine or (*b*) labelled glycerol. We chose the latter for two reasons: first [1-$^{14}$C]glycerol is readily available (The Radiochemical Centre, Amersham), whereas *o*-phenylenediamine would need to be prepared from [*ar*-$^{14}C_1$]aniline. Secondly, the subsequent conversion of [$^{14}$C]-1 : 10-phenanthroline into [$^{14}$C]-2 : 2′-dipyridyl would involve a loss of one-third of the radioactive carbon if the former originated from uniformly labelled aniline but not if it was prepared from [1-$^{14}$C]glycerol.

Unfortunately, a three- or four-fold excess of glycerol is usually employed in the Skraup reaction.[4] In a modification of the original procedure,[2] we were able to improve the reported yield (45%) by strict control of the conditions and substantially reduced the amount of glycerol without loss of yield, which amounted to 70% based on diamine and 44% based on glycerol.

[$^{14}$C]Phenanthroline was converted into [$^{14}$C]-2 : 2′-dipyridyl in 55% yield by oxidation [5] to [$^{14}$C]dipyridyl-3 : 3′-dicarboxylic acid and decarboxylation of the latter with copper powder in diphenyl at 200°.

*Experimental.*—A series of Skraup reactions essentially following Halcrow and Kermack's method [2] were carried out with *o*-phenylenediamine (2 g.). Different temperatures, times of reaction, and amounts of glycerol were tried with results shown in the Table. These results represent the mean of several experiments. In general, stirring improved the yield. There appeared to be an increase in yield of crude product as the amount of glycerol was reduced, but this may have been fortuitous.

| Temp. | Time (min.) | Glycerol (g.) | Yield † (%) | Temp. | Time (min.) | Glycerol (g.) | Yield † (%) |
|---|---|---|---|---|---|---|---|
| 130—140° | 120 | 10·8 * | 6 | 140—145° | 60 | 6·0 | 32 |
| 150—160 | 60 | 10·8 | 9 | 140—145 | 60 | 4·6 | 50 |
| 140—145 | 60 | 10·8 | 15 | 140—145 | 60 | 3·5 | tar, difficult |
| 140—145 | 75 | 10·7 | 14 | 140—145 | 60 | 1·8 | to solidify |
| 140—145 | 90 | 8·0 | 23 | | | | |

* 3 moles. † Based on glycerol.

[$^{14}$C]*Phenanthroline.* [1-$^{14}$C]glycerol (0·05 mc; 4·5 mg.; supplied by The Radiochemical Centre, Amersham), inactive glycerol (4·6 g.), *o*-phenylenediamine (2·0 g.), sulphuric acid (44 c.c.; 69%) and arsenic acid (10 c.c.; 80%) were heated for 60 min. at 140—145°. After cooling, water was added (60 c.c.) and then ammonia solution (120 c.c.; *d*, 0·88), and the mixture was set aside overnight. The tar was filtered off and dried. The filtrate was extracted with several portions of hot benzene; the tar was boiled for about 50 hr. with benzene. Evaporation of the solvent from the combined extracts left a brown granular solid (2·7 g.). The identity of this crude product (*A*) was established as follows (similarly prepared inactive material being used): (*a*) Spectrophotometric analysis as the deeply coloured ferrous complex [6] indicated that material (*A*) contained about 90% phenanthroline; possible impurities (*e.g.*, *o*-phenylenediamine, 8-aminoquinoline) are not likely to form strongly coloured ferrous complexes. (*b*) Distillation of (*A*) (3·1 g.) at 150—160°/0·1 mm. and subsequent crystallisation from water (charcoal) gave 1 : 10-phenanthroline hydrate (2·7 g.) (Found: C, 72·5; H, 5·05; N, 14·3. Calc. for $C_{12}H_{10}ON_2$: C, 72·7; H, 5·0; N, 14·2%). (*c*) Hydrated nickel nitrate (1 mole) and material (*A*) (3·5 moles) heated in aqueous solution gave a brown solution. This was extracted with ether and the remaining cherry-red aqueous solution evaporated slowly almost to dryness. The crystalline product was washed with a very small amount of cold water, alcohol, and finally chloroform (which removed a small amount of brown material). The spectrum of this dried product, obtained in very good yields, agreed exactly with that of authentic triphenanthrolinenickel(II) nitrate.

[$^{14}$C]-2 : 2′-*Dipyridyl.* Crude phenanthroline (2·3 g.) was converted into impure 2 : 2′-[$^{14}$C]-dipyridyl-3 : 3′-dicarboxylic acid by alkaline permanganate as described by Smith and Inglett.[5] We were not able to reproduce, consistently, the yields (80%) reported by these authors but our

[4] "Organic Reactions," Chapman and Hall Ltd., London, 1953, Vol. VII, p. 59.
[5] Smith and Inglett, *J. Amer. Chem. Soc.*, 1950, **72**, 842.
[6] Kolthoff, Leussing, and Lee, *ibid.*, p. 2173.

preparation was carried out on a similar scale. The product (1·8 g.) was not further purified but was well mixed with diphenyl (6·0 g.) and precipitated copper (1·0 g.; Hopkin and Williams), and the mixture heated at 190—210° until evolution of carbon dioxide ceased (about 20 min.). The cooled melt was removed from the reaction flask with cold methylated spirit, and after copper had been filtered off the solvent was removed. Dipyridyl was extracted from the residue by hot 2N-hydrochloric acid (about 100 c.c.) and the solution was boiled with animal charcoal. Sodium hydroxide was added to the filtered solution until crude dipyridyl (0·85 g.) was precipitated. A further 0·12 g. was obtained by extraction of the mother liquor with benzene. Light petroleum was added to this product, a small amount of insoluble impurity removed, and the filtrate evaporated almost to dryness. The crystalline residue (0·8 g.), m. p. 69—70° (Found: C, 75·5; H, 5·3; N, 17·7. Calc. for $C_{10}H_8N_2$: C, 76·9; H, 5·1; N, 17·9%), was shown to be pure 2 : 2′-dipyridyl by its ultraviolet spectra in methanol [7] and from the infrared spectra of the solid trisdipyridylnickel(II) nitrate when compared with samples obtained from "AnalaR" dipyridyl (m. p. 69—70°).

The radiochemical yield (92%) was determined by quantitative oxidation of the diluted glycerol and of the final pure complex to carbon dioxide, which was counted as "infinitely" thick barium carbonate samples.

We are grateful to the Department of Scientific and Industrial Research for a Maintenance Allowance (to M. J. G. W.) and to the University of Sheffield for an Alfred Tongue Scholarship (to P. E.).

THE UNIVERSITY, SHEFFIELD. [*Received, March 28th*, 1956.]

[7] Gillam, Hey, and Lambert, *J.*, 1941, 364.

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## 777. *Experiments with* 1 : 2 : 3 : 4-*Tetrahydro-3-methylquinazoline and Related Compounds.*

By A. R. OSBORN and K. SCHOFIELD.

DI- OR TETRA-HYDRO-1- AND -3-METHYLQUINAZOLINE appeared to be promising starting materials for synthesis of 1- and 3-methylquinazolinium salts. Mirza [1] reported that 3-methyl-4-quinazolone, on reduction with lithium aluminium hydride, gave either 1 : 2-dihydro-3-methyl-4-quinazolone or 1 : 2 : 3 : 4-tetrahydro-3-methylquinazoline as the main product, depending upon the conditions. The tetrahydro-compound, for which no properties were reported but of which the picrate (m. p. 156°) and methiodide were described, was synthesised from 2-aminobenzylmethylamine, but details of the synthesis were not given.

In the present work we found that 3-methyl-4-quinazolone, with an equimolecular amount of lithium aluminium hydride gave, not 3 : 4-dihydro-4-hydroxy-3-methylquinazoline, but a 60% yield of crystalline 1 : 2 : 3 : 4-tetrahydro-3-methylquinazoline. With excess of the reagent a better yield of the same product was obtained. The structure of this compound was confirmed by synthesis, of which we give details.

With lead tetra-acetate the tetrahydro-compound gave 3 : 4-dihydro-3-methylquinazoline (identical with a specimen prepared by the method of Gabriel and Colman [2]) or 3-methyl-4-quinazolone, depending on the conditions. Potassium ferricyanide produced only the latter product. Iodine in ethanol has been used to oxidise tetrahydro*iso*quinolines to quaternary salts,[3] but 1 : 2 : 3 : 4-tetrahydro-3-methylquinazoline consumed only one equivalent of this reagent, producing an equimolecular mixture of 3 : 4-dihydro-3-methylquinazoline and starting material. The same oxidising agent in the presence of silver acetate gave an inseparable mixture, whilst in large excess it produced 3-methyl-4-quinazolone.

With palladium–charcoal in boiling ethanol 3 : 4-dihydro-3-methylquinazoline gave none of the desired product, and potassium ferricyanide produced 3-methyl-4-quinazolone.

[1] Mirza, *Sci. and Cult.*, 1952, **17**, 530.
[2] Gabriel and Colman, *Ber.*, 1904, **37**, 3646.
[3] Haworth, *J.*, 1924, **1675**.

In the only successful experiment a poor yield of 3-methylquinazolinium hydroxide was obtained from the dihydro-compound by the action of excess of iodine in boiling butanol. It was later noticed that 3 : 4-dihydro-3-methylquinazoline was completely converted into 3-methyl-4-quinazolone when boiled in light petroleum, an observation according with the ready oxidation of 3-*p*-fluorophenyl-3 : 4-dihydroquinazoline recorded by Farrar.[4]

The more difficultly accessible 1-methyl-4-quinazolone [5] was reduced by lithium aluminium hydride to 1 : 2 : 3 : 4-tetrahydro-1-methylquinazoline, characterised as its picrate.

*Experimental.*—*2-Aminobenzylmethylamine.* When methyl-2-nitrobenzylamine [6] (4·66 g.), methanol (250 ml.), and 5% palladium–charcoal (2·5 g.) were shaken with hydrogen, reduction was complete in ½ hr. The filtered solution was evaporated under reduced pressure and the residue was distilled, giving the amine (3·0 g.), b. p. 114—118°/10 mm., as a very pale yellow oil. With alcoholic hydrochloric acid this gave the dihydrochloride, m. p. 218°. Busch [7] gave m. p. 217°.

1 : 2 : 3 : 4-*Tetrahydro-3-methylquinazoline.* The above diamine (0·3 g.), potassium hydroxide (0·2 g.), formaldehyde (excess of a 40% aqueous solution), and methanol (5 c.c.) were warmed for ½ hr. on the steam-bath. The cooled mixture was extracted with ether, and the dried ($Na_2SO_4$) extract was concentrated. The residue, on recrystallisation from light petroleum (b. p. 40—60°), gave colourless needles of 1 : 2 : 3 : 4-*tetrahydro-3-methylquinazoline*, m. p. 83—83·5 (Found : C, 73·2; H, 8·4. $C_9H_{12}N_2$ requires C, 72·9; H, 8·2%), identical with the compound described below. The *picrate*, m. p. 134° (Found : C, 47·6; H, 3·8. $C_9H_{12}N_2,C_6H_3O_7N_3$ requires C, 47·8; H, 4·0%), formed orange-yellow needles from ethanol.

*Reduction of 3-methyl-4-quinazolone.* (*a*) 3-Methyl-4-quinazolone (2 g.) in ether (100 c.c.) was added slowly to lithium aluminium hydride (1 mol.) in refluxing ether (50 c.c.) under nitrogen. A yellow solid was precipitated, and refluxing was continued for 4 hr. Water was added and the mixture was poured into excess of 2N-sulphuric acid. The organic layer was removed and combined with an ether extract of the acid layer. The sticky residue (0·025 g.) obtained from the ether was extracted with boiling light petroleum (b. p. 40—60°), leaving undissolved a white solid which formed colourless crystals, m. p. *ca.* 111°, from benzene–light petroleum. Sublimation (85°/0·1 mm.) raised the m. p. to 111—114°. The substance was probably 1 : 2-dihydro-3-methyl-4-quinazolone for which Mirza reported m. p. 115°. The original aqueous acid layer was neutralised with barium hydroxide solution, filtered, and extracted with ether. The dried ($Na_2SO_4$) extract provided a cream-coloured solid (0·87 g.) which from light petroleum (b. p. 40—60°) gave needles of 1 : 2 : 3 : 4-tetrahydro-3-methylquinazoline, m. p. 83°, identical with that above. Strong basification of the aqueous mother-liquor with potassium hydroxide, and continuous extraction with benzene, gave more (0·48 g.) of this compound.

(*b*) The reduction was repeated with the quinazolone (1·48 g.) and a two-fold excess of lithium aluminium hydride in ether (100 c.c.). The initial yellow precipitate slowly dissolved. After being refluxed for 6 hr. the solution was decomposed with water and dilute sulphuric acid. Basification of the acid layer and extraction with ether afforded the tetrahydro-compound (1·08 g.).

*Oxidation of 1 : 2 : 3 : 4-tetrahydro-3-methylquinazoline.* (*a*) The tetrahydro-compound (0·2 g.) in acetic acid (10 c.c.) at 70° was treated with lead tetra-acetate (1·22 g.), in portions during 5 min. The deep red solution formed initially became gradually lighter. It was set aside at room temperature for 2 hr. and then heated for 15 min. on the steam-bath. The mixture was poured into water (50 c.c.), and the basified solution was extracted continuously with benzene. Evaporation of the dried ($Na_2SO_4$) extract gave a pale yellow oil (0·095 g.) which crystallised. With picric acid this gave 3 : 4-dihydro-3-methylquinazoline picrate which from ethanol formed bright yellow prisms, m. p. 197—199° (Found : C, 48·4; H, 3·5. Calc. for $C_9H_{10}N_2,C_6H_3O_7N_3$ : C, 48·0; H, 3·5%), alone and mixed with a specimen obtained by the method of Gabriel and Colman.[8]

(*b*) A similar experiment with the tetrahydro-compound (0·2 g.) and lead tetra-acetate (2·5 g.) gave 3-methyl-4-quinazolone (0·04 g.), identified as its picrate (yellow needles from ethanol), m. p. and mixed m. p. 214°.

[4] Farrar, *J.*, 1954, 3253.
[5] Morley and Simpson, *J.*, 1949, 1354.
[6] Holmes and Ingold, *J.*, 1925, 1814.
[7] Busch, *J. prakt. Chem.*, 1895, **51**, 131.

(*c*) The tetrahydro-compound (0·295 g.) in absolute ethanol (15 c.c.) was heated on the steam-bath and treated dropwise with ethanolic iodine (2·55 g. in 50 c.c.) until the colour was no longer discharged (5 c.c. of the iodine solution were needed). The pale yellow solution deposited colourless crystals (0·195 g.; m. p. *ca.* 260°, giving a deep red melt) which were combined with the partly crystalline ether-insoluble residue (0·325 g.) obtained by evaporating the mother-liquor, dissolved in water, and strongly basified with 50% potassium hydroxide solution at 0°. Extraction with ether recovered a deliquescent solid (0·260 g.) which was treated with picric acid in ethanol. Fractional crystallisation of the product from methanol gave 3 : 4-dihydro-3-methylquinazoline picrate (0·21 g.), m. p. 197—199°, and 1 : 2 : 3 : 4-tetrahydro-3-methylquinazoline picrate (0·21 g.), m. p. 134°.

From an experiment carried out similarly, except that 4 equivs. of iodine were used, a poor recovery of a white solid (0·05 g.) was obtained. From this, boiling light petroleum removed 3-methyl-4-quinazolone (0·02 g.), identified as its picrate, and left undissolved a colourless solid (0·03 g.), m. p. 120—160°, which gave a neutral solution in water (3-methylquinazolinium hydroxide gives a strongly alkaline solution).

*Oxidation of* 3 : 4-*dihydro*-3-*methylquinazoline*. (*a*) The dihydro-compound (0·15 g.) in boiling butanol (10 c.c.) was treated with iodine (0·255 g.) in ethanol. The ethanol was boiled off and the butanol solution was refluxed for 3 hr., cooled, and poured into water. The mixture was basified with potassium hydroxide solution at 0° and extracted with ether. The solvent was removed from the dried ($CaSO_4$) extract *in vacuo* at 20° and the brown crystalline residue (0·1 g.) was boiled with ethyl acetate. A colourless solid (5 mg.; m. p. 195—220°) remained undissolved, and crystallisation of the ethyl acetate-soluble material from benzene gave colourless rhombs of 3-methylquinazolinium hydroxide (10 mg.), m. p. 163—165°, alone and mixed with a specimen prepared by the method of Schöpf and Oechler.[6]

(*b*) The dihydro-compound (0·18 g.) in water (2 c.c.) was added to 50% potassium hydroxide solution (1 c.c.) and then treated at −5° with potassium ferricyanide (0·3 g.) in water (2 c.c.). The mixture was shaken at −5° for 10 min. and filtered. The residue was washed with water, and the combined aqueous solution was repeatedly extracted with ether. Evaporation of the dried ($Na_2SO_4$) extract gave a solid (0·13 g.) which on recrystallisation from water gave 3-methyl-4-quinazolone m. p. 106°.

Three recrystallisations, from boiling light petroleum (b. p. 60—80°), of 3 : 4-dihydro-3-methylquinazoline resulted in the latter's complete conversion into 3-methyl-4-quinazolone.

1 : 2 : 3 : 4-*Tetrahydro*-1-*methylquinazoline*. 1-Methyl-4-quinazolone[5] (0·18 g.) was added by means of a Soxhlet apparatus to an excess of lithium aluminium hydride in ether (100 c.c.). The mixture was refluxed for 6 hr. and worked up by ether-extraction of the basified liquid in the usual way. The resulting brown oil did not crystallise and was converted into a picrate. Recrystallisation from ethanol gave orange-yellow crystals of 1 : 2 : 3 : 4-*tetrahydro*-1-*methylquinazoline picrate*, m. p. 161° (decomp.) (forming a red melt) (Found : C, 48·4; H, 3·9; N, 18·4. $C_9H_{12}N_2,C_6H_3O_7N_3$ requires C, 47·8; H, 4·0; N, 18·6%).

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PRINCE OF WALES ROAD, EXETER.

[*Received, April 25th*, 1956.]

[6] Schöpf and Oechler, *Annalen*, 1936, **523**, 1.

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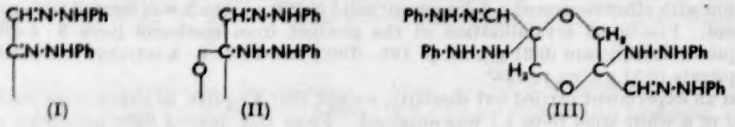
## 778. *The Ultraviolet Light Absorption of* 3-O-*Methylglycerosazone.*

By J. C. P. SCHWARZ and (in part) MAUREEN FINNEGAN.

BARRY, MCCORMICK, and MITCHELL [1] have recently confirmed and extended earlier semi-quantitative observations [2] that sugar osazones have very similar ultraviolet light absorption spectra. It has been suggested that these compounds have acyclic structures containing the chromophore (I), which may be chelated,[3] rather than cyclic structures containing the chromophore (II), which would necessitate the presence of 2 : 3- and 2 : 4-epoxide rings in glycerosazone and erythrosazone, respectively. However, the spectra of the sugar osazones differ appreciably from those of the bisphenylhydrazones of glyoxal and

[1] Barry, McCormick, and Mitchell, *J.*, 1955, 222.
[2] Engel, *J. Amer. Chem. Soc.*, 1935, **57**, 2419.
[3] Mester, *ibid.*, 1955, **77**, 4301.

methylglyoxal [1] (see Table), which contain the chromophore (I). Furthermore, glycerosazone may have the cyclic structure (III) which contains the chromophore (II), and erythrosazone may be represented by a 1 : 4-epoxide ring structure. In view of recent conflicting evidence regarding the structure of the osazones,[4] we have examined the spectrum of 3-*O*-methylglycerosazone, in which epoxide ring formation is impossible.




(I) (II) (III)

Attempts to prepare 3-*O*-methylglycerosazone from 2 : 3-di-*O*-methylglyceraldehyde diethyl acetal [5] gave unpromising results, but the osazone was readily obtained from 1-hydroxy-3-methoxypropanone, prepared by oxidation of 1-*O*-methylglycerol with bromine in the presence of sodium carbonate.[6] Its ultraviolet light absorption spectrum (see Table) was found to be very similar to those of the osazones examined by Barry, McCormick,

| 3-*O*-Methylglycerosazone | | Glycerosazone | | Methylglyoxal bisphenylhydrazone (from ref. 1) | |
|---|---|---|---|---|---|
| $\lambda_{max.}$ (mμ) | ε | $\lambda_{max.}$ (mμ) | ε | $\lambda_{max.}$ (mμ) | ε |
| 396 | 21,800 | 395 | 20,600 | 364 | 46,250 |
| 308—310 | 9,900 | 308—310 | 9,800 | 302—304 | 11,950 |
| 256—257 | 20,300 | 256 | 18,900 | — | — |

and Mitchell.[1] This suggests that the difference in spectrum between the sugar osazones and methylglyoxal bisphenylhydrazone should be ascribed to the $C_{(3)}$-oxygen function in the former compounds, rather than to epoxide-ring formation.

Barry, McCormick, and Mitchell [1] have shown that the molecular extinction coefficients of the sugar osazones at the maximum in the region 395—399 mμ lie within a narrow range ($\varepsilon_{max.}$ = 20,100—20,700) and they have used this fact to determine molecular weights. 3-*O*-Methylglycerosazone was found to absorb slightly more strongly in this region; redetermination of the spectrum of glycerosazone gave good agreement with the results of the above authors. Spectrophotometric determination of molecular weights may therefore be less accurate with 3-*O*-substituted osazones.

During the course of this work it was noted that alcoholic solutions of glycerosazone and 3-*O*-methylglycerosazone showed considerable changes in spectrum after exposure to daylight for 5 hours. These changes, which include displacement of the maxima at 395—396 mμ towards shorter wavelengths, occur more slowly in the dark.

*Experimental.*—Glycerosazone was prepared from glyceraldehyde diethylacetal and crystallised from benzene.

3-*O*-*Methylglycerosazone*. 1-*O*-Methylglycerol [7] (11 g.) and anhydrous sodium carbonate (13 g.) in water (60 c.c.) were treated at 10° with bromine (4·8 c.c.), added in one portion with shaking. After 2 hr. the solution was acidified and the excess of bromine was destroyed with sulphur dioxide. The solution was then brought to pH 4 and treated with an aqueous solution of phenylhydrazine hydrochloride (5 g.) and sodium acetate (7 g.). After 24 hr. at 35°, the resulting tarry solid was separated by filtration. Crystallisation from benzene yielded 3-*O*-*methylglycerosazone* (0·85 g.); more (0·3 g.) was obtained by chromatography of the benzene mother-liquor on alumina. Three crystallisations from methanol yielded needles, m. p. 140—142° (Found: C, 68·2; H, 6·3; N, 19·5; OMe, 10·8. $C_{16}H_{16}ON_4$ requires C, 68·1; H, 6·4; N, 19·9; OMe, 11·0%). The m. p. and spectrum were unchanged by further crystallisation.

*Light-absorption measurements*. These were made on a Unicam SP 500 spectrophotometer with 1 cm. quartz cells and freshly prepared solutions of the osazones in 95% aqueous ethanol. The maxima were determined before the remainder of the spectrum.

[4] Aspinall and Schwarz, *Ann. Reports*, 1955, **52**, 255.
[5] Rothstein, *J.*, 1940, 1560.
[6] Neuberg, *Biochem. Z.*, 1931, **238**, 459.
[7] Grün and Bockisch, *Ber.*, 1908, **41**, 3465.

The authors are grateful to Professor E. L. Hirst, F.R.S., for advice and encouragement and to Dr. V. C. Barry for helpful discussion. One of them (J. C. P. S.) thanks the University of Edinburgh for the award of an I.C.I. Fellowship.

DEPARTMENT OF CHEMISTRY, THE UNIVERSITY, EDINBURGH, 9. [*Received, May 18th*, 1956.]

## 779. *Reduction of Amides by Lithium Borohydride.*

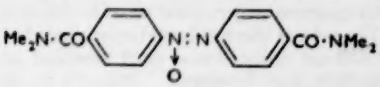
By M. DAVIS.

AMIDES are readily reduced to amines by lithium aluminium hydride, but not by sodium or potassium borohydride; lithium borohydride has not been extensively investigated in this connection.

Bailey [1] found that 2-acetamidoethanol gave only 1·5% of 2-ethylaminoethanol when treated with lithium borohydride in boiling tetrahydrofuran for 3 hours, and concluded that there was little risk of amide reduction with sparingly soluble peptides. On the other hand, Crawhall and Elliott [2] have demonstrated that certain peptides can undergo cleavage under similar conditions, with formation of the corresponding alcohol and amine. Wittig and Hornberger [3] found that some tertiary *N*-carbazolyl-amides of cinnamic acid and its vinylogues when treated with a limited amount (0·25 mol.) of lithium borohydride in boiling ether, gave some of the corresponding aldehyde, but that *NN*-dimethyl-, *NN*-methylphenyl-, and *NN*-diphenyl-amides were usually unaffected.

I have examined the behaviour of benzamide, *N*-methylbenzamide, and *NN*-dimethylbenzamide towards excess of lithium borohydride (1·1 mol.; prepared *in situ* from potassium borohydride and lithium chloride [4, 5]) in boiling tetrahydrofuran. The primary and secondary amides were recovered, but the tertiary amide was completely reduced to a mixture of *NN*-dimethylbenzylamine (33%) and benzyl alcohol (58%). The preparation of benzyl alcohol from *NN*-diethylbenzamide by using lithium aluminium hydride has been recorded by Nystrom and Brown,[6] but this reduction was carried out under conditions which favoured the formation of aldehyde rather than of amine.[7]

Previous workers have shown that the nitro-group does not normally interfere in the reduction of other groups by lithium borohydride, although Nystrom, Chaikin, and Brown [8] found that nitrobenzene gave 22% of aniline, 30% of unidentified oil, and 30% of unchanged material with the reagent in boiling ether–tetrahydrofuran, whilst Brown, Mead, and Subba Rao [5] reported that a vigorous reaction occurred with nitrobenzene in diethylene glycol dimethyl ether at 100°, but they made no attempt to characterise the products.



(I)

Treatment of *NN*-dimethyl-*p*-nitrobenzamide with lithium borohydride in boiling tetrahydrofuran gives the corresponding azoxy-compound (I) (41%) together with a neutral oil which is largely *p*-nitrobenzyl alcohol (52%). The structure assigned to (I) has been confirmed by further reduction with stannous chloride to *p*-amino-*NN*-dimethylbenzamide, and by independent synthesis from the known *pp'*-dicarboxyazoxybenzene.

*Experimental.—Reduction of* NN-*dimethylbenzamide.* Lithium chloride (4·66 g.; dried at 120°) was added to a stirred mixture of *NN*-dimethylbenzamide (14·9 g.) and potassium borohydride (5·94 g.) in anhydrous tetrahydrofuran (60 ml.). The mixture was refluxed for 20 hr., then cooled, diluted with water, and extracted with ether (3 × 150 ml.). The ether solution

[1] Bailey, *Biochem. J.*, 1955, **60**, 170.
[2] Crawhall and Elliott, *Nature*, 1955, **175**, 299.
[3] Wittig and Hornberger, *Annalen*, 1952, **577**, 11.
[4] Paul and Joseph, *Bull. Soc. chim. France*, 1952, 550; Kollonitsch, Fuchs, and Gabor, *Nature*, 1954, **173**, 125.
[5] Brown, Mead, and Subba Rao, *J. Amer. Chem. Soc.*, 1955, **77**, 6209.
[6] Nystrom and Brown, *ibid.*, 1948, **70**, 3738.
[7] Brown, *Organic Reactions*, 1951, **6**, 479.
[8] Nystrom, Chaikin, and Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 3245.

was washed with 2N-hydrochloric acid (2 × 50 ml.) and water, dried, and evaporated. The residue (6·3 g.) was benzyl alcohol, identified (mixed m. p.) as the *p*-nitrobenzoate, m. p. 84—86° (lit.,[9] m. p. 85°). The acid extract was basified and extracted with ether (2 × 100 ml.), and the washed and dried extract was evaporated, giving *NN*-dimethylbenzylamine (4·5 g.), identified (mixed m. p.) as the picrate, m. p. 95·5—96·5° (lit.,[10] 96°), and the methiodide, m. p. 179—181° (lit.,[11] 179°).

*Reduction of* NN-*dimethyl*-p-*nitrobenzamide*. Dry lithium chloride (2·26 g.) was added to a stirred mixture of *NN*-dimethyl-*p*-nitrobenzamide (9·4 g.) and potassium borohydride (2·88 g.) in anhydrous tetrahydrofuran (60 ml.). The mixture was refluxed for 20 hr., cooled, diluted with water, and filtered from pp′-*di*(*dimethylcarbamoyl*)*azoxybenzene* (3·35 g.; m. p. 211—216°), which separated from ethanol in orange plates, m. p. 214—216° [Found: C, 63·7; H, 6·05; N, 16·4%; *M*, 310 (in acetone). $C_{18}H_{22}O_3N_4$ requires C, 63·5; H, 5·9; N, 16·5%; *M*, 340]. [$\lambda_{max.}$ in EtOH: 272 (ε 10,700) and 332 mμ (ε 19,800); shoulder at 300 mμ (ε 14,100)]. Extraction of the original filtrate with ether gave a neutral oil (3·8 g.) which was largely *p*-nitrobenzyl alcohol and was identified (mixed m. p.) as the *p*-nitrobenzoate, m. p. 169—170° (lit.,[12] m. p. 168—168·5°). Further reduction of this azoxy-compound (1 g.) with stannous chloride dihydrate (4 g.) in concentrated hydrochloric acid (8 ml.) gave *p*-amino-*NN*-dimethylbenzamide, m. p. 152—153°, not depressed by an authentic specimen (lit.,[13] m. p. 153°). The *picrate* had m. p. 207—209°, not depressed by an authentic specimen, m. p. 208—210° (Found: C, 45·8; H, 4·15; N, 17·5. $C_9H_{12}ON_2.C_6H_3O_7N_3$ requires C, 45·8; H, 3·8; N, 17·8%).

*Synthesis of* pp′-*di*(*dimethylcarbamoyl*)*azoxybenzene*. *pp′*-Dicarboxyazoxybenzene, prepared as described by Bacharach and Weinstein [14] and recrystallised from dimethylformamide, did not melt <360°. A mixture of this acid (1 g.) and thionyl chloride (25 ml.) was refluxed for 7 hr., the filtered solution was evaporated, and the residue was warmed for 15 min. at 100° with aqueous dimethylamine (25%; 20 ml.). Recrystallisation of the product from ethanol gave the dimethylamide, m. p. 215—217°, mixed m. p. 215—216·5° (Found: C, 63·8; H, 6·35; N, 16·4%).

The author thanks Dr. H. J. Barber, F.R.I.C., for the suggestion which prompted these experiments, Mr. S. Bance, B.Sc., A.R.I.C., for the semi-microanalyses, Dr. D. F. Muggleton for the absorption spectrum, and the Directors of May and Baker Ltd. for permission to publish these results.

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Dagenham, Essex.

[*Received, May 28th*, 1956.]

[9] Meisenheimer and Schmidt, *Annalen*, 1929, **475**, 175.
[10] Von Braun, Kühn, and Goll, *Ber.*, 1926, **59**, 2335.
[11] Emde, *Arch. Pharm.*, 1909, **247**, 353.
[12] Lyons and Reid, *J. Amer. Chem. Soc.*, 1917, **39**, 1735.
[13] Wenker, *ibid.*, 1938, **60**, 1081.
[14] Bacharach and Weinstein, *Rec. Trav. chim.*, 1935, **54**, 931.

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## 780. (+)-β-*Aminobutyric Acid*; *the Correlation of its Configuration with that of* α-*Amino-acids*.

By K. Balenović, N. Bregant, and D. Cerar.

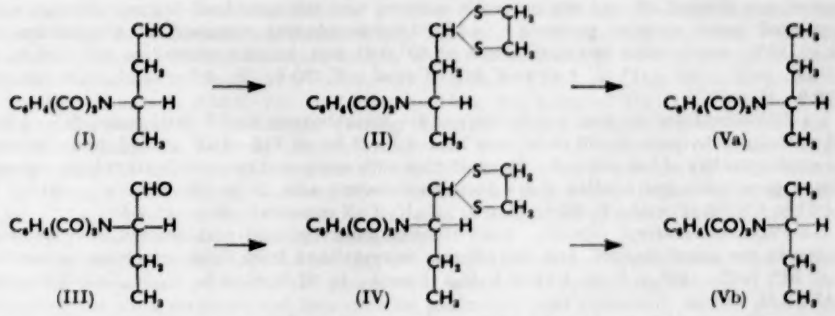
β-Aminobutyric acid was first resolved into optical antipodes by Fischer and Scheibler.[1] A few years ago the (+)-antipode was prepared from L-alanine [2] by application of the Arndt–Eistert reaction. Wolff rearrangement of diazo-ketones used in the Arndt–Eistert procedure is known to proceed with retention of configuration when the rearrangement occurs at an asymmetric centre;[3] therefore (+)-β-aminobutyric acid was presumed to be of the L-configuration.*

In the present paper a description is given of the direct chemical correlation of configuration of (+)-β-aminobutyric acid with L-α-aminobutyric acid.

* In this paper, L is used in an extension of the convention for α-amino-acids to β-amino-acids.

[1] Fischer and Scheibler, *Annalen*, 1911, **383**, 337.
[2] Balenović, Cerar, and Fuks, *J.*, 1952, 3316.
[3] Lane, Willenz, Weissberger, and Wallis, *J. Org. Chem.*, 1940, **5**, 276.

(+)-β-Aminobutyric acid was converted into (+)-β-phthalimidobutyraldehyde (I) and its ethylene mercaptal (II). Analogous reactions were applied to the preparations of L-α-phthalimidobutyraldehyde (III) and its ethylene mercaptal (IV) prepared from L-α-aminobutyric acid. Desulphurisation [4] of the mercaptals (II) and (IV) with Raney nickel of low activity, in acetone,[5] gave the hitherto undescribed (+)-2-phthalimidobutane (Va) with $[\alpha]_D$ +34°, and (−)-2-phthalimidobutane (Vb) with $[\alpha]_D$ −32°.



(+)-β-Aminobutyric acid is therefore of the L-configuration, as was expected. Consequently, in the recently suggested terms [6] (+)-2-phthalimidobutane would now be (*S*)-2-phthalimidobutane, and the (−)-antipode would be (*R*)-2-phthalimidobutane.

Catalysts of higher activities than used in earlier similar desulphurisations [7] afforded 2-(hexahydrophthalimido)butanes.

*Experimental.*—(+)-β-*Phthalimidobutyric acid.* A solution of methyl (+)-β-phthalimidobutyrate [2] (3·2 g.) in acetic acid (18 c.c.) was treated with 48% hydrobromic acid (36 c.c.) and kept at 40—50° during 3 hr., with stirring. After cooling, water was added (100 c.c.) and the mixture extracted with benzene in the usual manner. The extracts were evaporated to dryness, and an oily residue of (+)-β-*phthalimidobutyric acid* (2·4 g., 80%) was obtained, which crystallised on addition of a small quantity of benzene. Recrystallisation from the same solvent gave white needles of the pure compound, m. p. 80° $[\alpha]_D^{19}$ +43 ± 1° (*c*, 1·61 in $C_6H_6$) (Found: C, 61·7; H, 4·9. $C_{12}H_{11}O_4N$ requires C, 61·8; H, 4·8%).

(+)-β-*Phthalimidobutyryl chloride.* A solution of the acid (2 g.) in thionyl chloride (15 c.c.) was left at room temperature overnight; the excess of thionyl chloride was then removed under reduced pressure and the oily residue of (+)-β-*phthalimidobutyryl chloride* (1·9 g., 88%) dissolved in benzene, from which white needles were obtained by precipitation with light petroleum (b. p 40—60°). Repeated recrystallisation from benzene–light petroleum yielded the pure compound, m. p. 92° and $[\alpha]_D^{20}$ +65° ±2° (*c*, 0·43 in $C_6H_6$) (Found: C, 57·1; H, 4·0. $C_{12}H_{10}O_3NCl$ requires C, 57·3; H, 4·0%).

(+)-β-*Phthalimidobutyraldehyde* (I). A solution of (+)-β-phthalimidobutyryl chloride (4·6 g., 0·02 mole) in xylene (20 c.c.) was reduced by the Rosenmund–Zetzsche procedure [8] with palladium (5%) on barium sulphate at 110—115°. After 5 hr. 0·70 mol. of hydrogen chloride had been evolved. The catalyst was filtered off, and the mixture evaporated *in vacuo* until crystallisation started (7—8 c.c.). (+)-β-*Phthalimidobutyraldehyde* (1·8 g., 46%), after recrystallisation from benzene–light petroleum or sublimation at 110°/0·016 mm., formed needles, m. p. 113°, $[\alpha]_D^{29}$ +68° ± 2° (*c*, 0·52 in $C_6H_6$) (Found: C, 65·9; H, 5·1. $C_{12}H_{11}O_3N$ requires C, 66·3; H, 5·1%).

(+)-β-*Phthalimidobutyraldehyde ethylene mercaptal* (II). The aldehyde (0·8 g.; $[\alpha]_D$ +47°) and ethanedithiol (0·5 c.c.) were dissolved in a 3% solution of anhydrous hydrochloric acid in dioxan (15 c.c.). After 3 days at room temperature, the solvent was removed *in vacuo*. The

[4] Bougault, Cattelain, and Chabrier, *Bull. Soc. chim. France*, 1938, **5**, 1699; 1940, **7**, 780.
[5] Cf. Spero, McIntosh, jun., and Levin, *J. Amer. Chem. Soc.*, 1948, **70**, 1907.
[6] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81.
[7] Cf., *e.g.*, Mozingo, Wolf, Harris, and Folkers, *J. Amer. Chem. Soc.*, 1943, **65**, 1013; Wolfrom, Lemieux, and Olin, *ibid.*, 1949, **71**, 2870.
[8] Cf., *e.g.*, Mosettig and Mozingo, *Organic Reactions*, 1948, **4**, 368.

oily residue of *mercaptal* was dissolved in benzene (20 c.c.), filtered through alumina (10 g.), and washed with the same quantity of benzene. After evaporation of the combined filtrates *in vacuo*, a clear oil (0·9 g., 80%), $[\alpha]_D$ +41° ± 1° (unchanged after distillation at 130°/0·005 mm.), was obtained (Found: C, 57·6; H, 5·2. $C_{14}H_{15}O_2NS_2$ requires C, 57·3; H, 5·2%).

(+)-2-*Phthalimidobutane* (Va). A solution of the foregoing mercaptal (0·5 g., $[\alpha]_D$ +41°) in acetone [8] (15 c.c.) was heated with Raney nickel (7 g.; W-1 activity; [9] kept under 96% ethanol for 1 month before use) under reflux with stirring during 7 hr., then cooled. The catalyst was filtered off and washed with acetone, and the combined acetone filtrates were evaporated under reduced pressure. (+)-2-*Phthalimidobutane* remained as a colourless oil (0·3 g., 86%) which after two distillations at 60°/0·01 mm. became crystalline and had m. p. 33—35°, $[\alpha]_D^{18}$ +34° ± 1° (*c*, 1·43 in $C_6H_6$) (Found: C, 70·9; H, 6·7. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·5%).

L-α-*Phthalimidobutyric acid*. A mixture of L-α-aminobutyric acid [10] (0·03 mole; $[\alpha]_D$ +20°) and phthalic anhydride (0·033 mole) was heated for 2 hr. at 115—120°, cooled, and dissolved in a small quantity of hot ethanol. Precipitation with water and recrystallisation from aqueous ethanol gave colourless needles of L-α-*phthalimidobutyric acid*, m. p. 73—75°, $[\alpha]_D$ −31° ± 1° (*c*, 1·71 in EtOH) (Found: C, 62·0; H, 5·0. $C_{12}H_{11}O_4N$ requires C, 61·8; H, 4·8%).

L-α-*Phthalimidobutyryl chloride*. L-α-Phthalimidobutyric acid and thionyl chloride were treated in the usual manner, and the *chloride* recrystallised from light petroleum as needles, m. p. 58°, $[\alpha]_D^{20}$ −59° ± 1° (*c*, 1·19 in $C_6H_6$) (Found: C, 57·5; H, 4·2. $C_{12}H_{10}O_3NCl$ requires C, 57·3; H, 4·0%).

(−)-α-*Phthalimidobutyraldehyde* (III) was prepared in the same manner as the inactive compound,[11] in 35% yield, with m. p. 83—84°, $[\alpha]_D^{20}$ −37° ± 1°) (*c*, 1·41 in $C_6H_6$) (Found: C, 66·3; H, 5·3. $C_{12}H_{11}O_3N$ requires C, 66·4; H, 5·1%).

This aldehyde (2·9 g.; $[\alpha]_D$ −32°) was converted into the *ethylene mercaptal* in the same manner as the β-compound (yield, 2·35 g., 60%), and after several recrystallisations from ethanol formed prisms, m. p. 121—122°, $[\alpha]_D^{17}$ +34° ± 1° (*c*, 1·61 in EtOH) (Found: C, 57·4; H, 5·2. $C_{14}H_{15}O_2NS_2$ requires C, 57·3; H, 5·2%).

(−)-2-*Phthalimidobutane* (Vb). The preceding mercaptal (0·5 g.; $[\alpha]_D$ +32°) was desulphurized in the same manner as the β-compound. The (−)-2-*phthalimidobutane* (0·3 g., 86%) thus obtained, after distillation at 60°/0·01 mm., had m. p. 33—35°, $[\alpha]_D^{18}$ −32° ± 1° (*c*, 1·81 in $C_6H_6$) (Found: C, 71·0; H, 6·4. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·5%).

A mixture of equal quantities (10 mg.) of pure (+)- and (−)-2-phthalimidobutanes with m. p.s 33—35° was distilled at 60°/0·01 mm. The distillate solidified in long needles, was optically inactive, and had m. p. 24—25°, as described earlier [12] for racemic 2-phthalimidobutane.

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[*Received, June 8th*, 1956.]

[9] Adkins and Covert, *J. Amer. Chem. Soc.*, 1932, **54**, 4116.
[10] Birnbaum, Levintow, Kingsley, and Greenstein, *J. Biol. Chem.*, 1952, **194**, 455.
[11] Balenović, Bregant, Galijan, Štefanac, and Škarić, *J. Org. Chem.*, 1956, **21**, 115.
[12] Mumm and Richter, *Ber.*, 1940, **73**, 843.

# OBITUARY NOTICE.

## ARTHUR LANDAUER STERN

**1867—1956**

Arthur Landauer Stern was educated at King Edward's School, Birmingham, and Mason College (now the University of Birmingham). Graduating (B.Sc., London) with First Class Honours he became Tangye Research Scholar under Tilden until, in 1889, he commenced work as private assistant to Cornelius O'Sullivan at Burton-on-Trent. In this capacity he worked in the field of sugars, starch, etc., and later, in 1894, was awarded the D.Sc. (London) for a thesis on the chemistry of cellulose. Joining the brewing staff of Bass, Ratcliff & Gretton he worked on much the same subjects together with that of the nutrition of yeast. Papers appearing at this time included one on cellulose (*Trans.*, 1895, 74) and one on "The Identity of Dextrose from Different Sources, etc." (O'Sullivan and Stern, *Trans.*, 1896, 69, 1691). Later "The Nutrition of Yeast" received attention in four papers (*Trans.*, 1898, 73, 182; 1901, 79, 943; *J. Inst. Brewing*, 1899, 399; 1902, 690).

During the years which followed his appointment in 1906 as head brewer at the New Brewery (Bass) his new duties prevented the prosecution and publication of original work, but Stern instigated the work on yeast and fermentation performed (and published) by the late Arthur Slator, D.Sc. Improvements in brewing technology were devised, particularly in connection with the chilling and filtration of bottled beer for export. He was an original member of the Institute of Brewing.

He retired from active work in 1924 and most of the generation who knew him personally are no longer living. In his younger days he played croquet but he remained an enthusiastic golfer until the end. He leaves two sons, both in the medical profession, and five daughters.

Reginald Haydn Hopkins.

# *Reactions of Radicals in Gaseous Systems.*

THE LIVERSIDGE LECTURE, DELIVERED AT THE ROYAL INSTITUTION, ALBEMARLE STREET, LONDON W.1, ON DECEMBER 1ST, 1955, AND IN LEEDS ON NOVEMBER 17TH, 1955, AND ABERDEEN ON NOVEMBER 24TH, 1955.

By E. W. R. STEACIE.

In the last 25 years it has become apparent that free radicals play a major part in most gas-phase reactions of simple organic molecules. There is no question that most photochemical reactions of this type involve radicals. The work of Sir Cyril Hinshelwood and his school makes it probable that hydrocarbon decompositions do not proceed entirely by a free-radical mechanism, but certainly free radicals play a prominent part in these reactions and in other organic decompositions.

Rice has proposed a type of mechanism for organic decompositions which is certainly largely valid in principle. There are, however, many discrepancies in specific cases. As a result it has become very important to investigate the chemical reactions of organic free radicals in the gas phase. If the rates of such reactions could be determined unambiguously it would be possible to make many detailed predictions about the overall mechanisms of organic reactions.

The main problem in investigating the rates of free-radical reactions is that the radicals have to be prepared *in situ*, and there is thus some uncertainty about their identity, purity, and especially their concentration. It is usually impossible to determine radical concentrations directly, and it is therefore necessary to compare ratios of rates, or to use some indirect yardstick as a measure of the radical concentration. In general, photochemical methods of producing radicals for such investigations are to be preferred since it is possible in this way to vary the temperature independently of the rate of production of radicals, and to work at much lower temperatures. The investigation of the rates of elementary organic reactions has therefore become one of the major tasks of photochemistry.

*Types of Elementary Reaction.*—A typical Rice mechanism (which is certainly over-simplified) is that for the ethane decomposition :

$$C_2H_6 \longrightarrow 2CH_3 \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$CH_3 + C_2H_6 \longrightarrow CH_4 + C_2H_5 \quad . \quad . \quad . \quad (2)$$

$$C_2H_5 \longrightarrow C_2H_4 + H \quad . \quad . \quad . \quad (3)$$

$$H + C_2H_6 \longrightarrow C_2H_5 + H_2 \quad . \quad . \quad . \quad (4)$$

$$H + C_2H_5 \longrightarrow C_2H_6 \quad . \quad . \quad . \quad . \quad (5)$$

$$\text{or} \longrightarrow C_2H_4 + H_2 \quad . \quad . \quad . \quad (6)$$

There are thus several distinct types of free-radical reaction which need investigation. Reaction (1) is essentially a question of bond dissociation energies. Reaction (3) is a radical decomposition. Reactions (2) and (4) are metatheses which involve the transfer of a hydrogen atom from a molecule to a radical. Reactions (5) and (6) involve the recombination and disproportionation of two radicals. In this lecture I propose to review the present status of our knowledge of hydrogen-transfer reactions, recombination, and disproportionation.

*The Acetone Photolysis.*—In choosing a substance as a photochemical source of radicals it is obviously desirable to pick one whose photochemical behaviour has been well investigated. A favourite choice is acetone, which, following on the pioneer work of Norrish, has been much investigated by Noyes and his collaborators. Acetone absorbs from about 3300 Å down to shorter wavelengths. It is too complex a molecule to be very promising from a spectroscopic point of view, and I will not discuss its spectrum, or its very interesting fluorescence properties. Its photochemical decomposition has been much investigated between 3130 Å and 2537 Å. The list of free-radical reactions which are definitely involved in its photolysis is formidable, *viz.*,

$$CH_3{\cdot}CO{\cdot}CH_3 + h\nu \longrightarrow CH_3 + CH_3{\cdot}CO \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$CH_3 + CH_3{\cdot}CO \longrightarrow CH_3{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$CH_3 + CH_3 \longrightarrow C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$CH_3{\cdot}CO + CH_3{\cdot}CO \longrightarrow (CH_3{\cdot}CO)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$CH_3{\cdot}CO \longrightarrow CH_3 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$CH_3 + CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow CH_4 + CH_2{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad (12)$$

$$CH_3 + CH_2{\cdot}CO{\cdot}CH_3 \longrightarrow C_2H_5{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

$$2CH_2{\cdot}CO{\cdot}CH_3 \longrightarrow (CH_2{\cdot}CO{\cdot}CH_3)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

$$CH_2{\cdot}CO{\cdot}CH_3 \longrightarrow CH_2{\cdot}CO + CH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

$$CH_3 + CH_2{\cdot}CO \longrightarrow CH_4 + CH_2{\cdot}CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

$$CH_3{\cdot}CO + CH_3{\cdot}CO \longrightarrow CH_2{\cdot}CHO + CH_2{\cdot}CO \quad . \quad . \quad . \quad . \quad (17)$$

The usual way of dealing with such a mechanism is the so-called steady-state method. In this we equate the rate of change of concentration of the short-lived species to zero in the steady state and solve the resulting equations. This has two disadvantages in the present case. In the first place the mechanism must be complete, and we are by no means certain that there are no other part reactions involved. Also, with 11 part reactions the resulting equations would be exceedingly complex and impossible to apply to the results.

The situation is not, however, nearly as bad as it looks. Reaction (8) merely lowers the quantum yield, and provided we are dealing with ratios of products it can be neglected. Acetyl is unstable, and at temperatures above 100° or 120° it is legitimate in the absence of highly reactive added substances to write (7) as

$$CH_3{\cdot}CO{\cdot}CH_3 + h\nu \longrightarrow 2CH_3 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7a)$$

and to neglect all reactions involving $CH_3{\cdot}CO$, *viz.*, (8), (10), (11), (16), and (17). Also, reaction (15) is only of importance at quite high temperatures. Hence in the range 100—300° it is almost always permissible merely to write the mechanism as:

$$CH_3{\cdot}CO{\cdot}CH_3 + h\nu \longrightarrow 2CH_3 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7a)$$

$$CH_3 + CH_3 \longrightarrow C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$CH_3 + CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow CH_4 + CH_2{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad (12)$$

$$CH_3 + CH_2{\cdot}CO{\cdot}CH_3 \longrightarrow C_2H_5{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

$$2CH_2{\cdot}CO{\cdot}CH_3 \longrightarrow (CH_2{\cdot}CO{\cdot}CH_3)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

It may, however, be profitable to give a word of warning about simplified mechanisms at this point. All possible part reactions will always occur to some extent. In certain circumstances it will be possible to ignore many of them. It should be emphasized, however, that the resultant simple mechanisms will only hold over limited ranges of the experimental parameters. One should always be cautious in applying a simple mechanism when the conditions have been drastically changed with regard to temperature, concentration, intensity, presence of foreign gases, and so on.

*Hydrogen-abstraction reactions.*

In the temperature range 100—300° a mass of information has been obtained about hydrogen-abstraction reactions by the following method. In this range the only reaction forming ethane is (9) and the only reaction forming methane is (12). Hence, where $R_x$ represents the rate of formation of the product $x$, and Ac represents acetone,

$$R_{C_2H_6} = k_9[CH_3]^2$$

$$R_{CH_4} = k_{12}[CH_3][Ac]$$

Hence $$k_{12}/k_9^{\frac{1}{2}} = R_{CH_4}/(R_{C_2H_6}^{\frac{1}{2}}[Ac])$$

It is thus possible to evaluate $k_{12}/k_9^{\frac{1}{2}}$. If now a foreign gas RH is added, methane will also be produced by

$$CH_3 + RH \longrightarrow CH_4 + R \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

Hence, provided that there is still no other method of forming $CH_4$ and $C_2H_6$,

$$R_{CH_4} = k_{12}[CH_3][Ac] + k_{18}[CH_3][RH]$$

$$R_{C_2H_6} = k_9[CH_3]^2$$

Hence $$R_{CH_4}/R_{C_2H_6}^{\frac{1}{2}} = k_{12}[Ac]/k_9^{\frac{1}{2}} + k_{18}[RH]/k_9^{\frac{1}{2}}$$

Since $k_{12}[Ac]/k_9^{\frac{1}{2}}$ is known, we can evaluate $k_{18}/k_9^{\frac{1}{2}}$. It thus becomes possible to determine the rates of reaction (18) for a series of organic compounds relative to the rate of recombination of methyl radicals. Actually, as we shall see later, the rate of recombination of methyl radicals has now been determined, so that it is possible to arrive at absolute values of the rate constants of reactions of the type of (18).

An alternative approach is to use deuteroacetone, and compare the rate of (19) with that of (20).

$$CD_3 + CD_3{\cdot}CO{\cdot}CD_3 \longrightarrow CD_4 + CD_3{\cdot}CO{\cdot}CD_2 \quad . \quad . \quad . \quad . \quad . \quad (19)$$

$$CD_3 + RH \longrightarrow CD_3H + R \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (20)$$

By these methods the rates of a large number of hydrogen-abstraction reactions have been measured in recent years.[1] By carrying out the investigation over a range of temperatures we can determine the activation energy and the pre-exponential factor as expressed by the Arrhenius equation $k = Ae^{-E/RT}$, or, if we put $A = PZ$, where $Z$ is the collision number and $P$ is the so-called steric factor, the results can be given in the form of activation energies and steric factors.

A few typical results for a series of hydrocarbons are given in Table 1. Recent unpublished results by Kutschke indicate that some of the activation energies in the Table are somewhat

TABLE 1. *The abstraction of hydrogen atoms by methyl radicals from the photolysis of acetone.*
(Trotman-Dickenson and Steacie.[2])

| Compound | $E_{18} - \frac{1}{2}E_9$ (kcal.) | $k_{18}/k_9^{\frac{1}{2}} \times 10^{13}$ * at 182° c. | $P_{18}/P_9^{\frac{1}{2}} \times 10^4$ | Number of "active" H- atoms | $k_{18}/k_9^{\frac{1}{2}} \times 10^{13}$ * at 182° c. per "active" H-atom |
|---|---|---|---|---|---|
| Ethane | 10·4 | 3·8 | 6 | 6 | 0·6 |
| 2 : 2-Dimethylpropane | 10·0 | 6·3 | 6 | 12 | 0·5 |
| 2 : 2 : 3 : 3-Tetramethylbutane... | 9·5 | 10·0 | 7 | 18 | 0·6 |
| *n*-Butane | 8·3 | 21 | 3 | 4 | 4·5 |
| *n*-Pentane | 8·1 | 27 | 3 | 6 | 4·0 |
| *n*-Hexane | 8·1 | 33 | 3 | 8 | 3·8 |
| 2-Methylpropane | 7·6 | 42 | 3 | 1 | 37 |
| 2 : 3-Dimethylbutane | 7·8 | 78 | 6 | 2 | 36 |
| 2 : 3 : 4-Trimethylpentane | 7·9 | 65 | 8 | 3 | 20 |
| Ethene | 10·0 | 5·6 | 9 | 4 | 1·4 |
| Propene | 7·7 | 23 | 3 | 3 | 8 |
| But-2-ene | 7·7 | 57 | 7 | 6 | 10 |
| 2-Methylpropene | 7·3 | 49 | 4 | 6 | 8 |
| 2 : 3-Dimethylbut-2-ene | 7·8 | 145 | 17 | 12 | 12 |
| But-1-ene | 7·6 | 66 | 8 | 2 | 33 |
| Pent-1-ene | 7·6 | 68 | 8 | 2 | 34 |
| 3-Methylbut-1-ene | 7·4 | 102 | 9 | 1 | 102 |
| *cyclo*Propane | 10·3 | 2·1 | 4 | 6 | 0·4 |
| *cyclo*Butane | 9·3 | 22 | 17 | 8 | 2·8 |
| *cyclo*Pentane | 8·3 | 47 | 9 | 10 | 4·7 |
| *cyclo*Hexane | 8·3 | 42 | 8 | 12 | 3·7 |
| Benzene | 9·2 | 1·9 | 1 | 6 | 0·3 |
| Toluene | 8·3 | 26 | 5 | 3 | 8·7 |
| Acetone | 9·7 | 19 | 10 | 6 | 3·2 |

* Units of quantities entering into $k$ are molecules, cm.$^3$, and seconds.

low, as are the steric factors. The differences are not great enough to change the trend of the results, although they somewhat increase the scatter. The differences in $A$ and $E$ compensate one another, however, and the rate constants at a given temperature are little affected.

One result that is apparent is that the steric factors of these reactions are low, of the order of $10^{-3}$. It has frequently been assumed in the past that such steric factors are approximately unity. It is obvious that this is not the case, and that the mere determination of an activation energy gives only a very vague idea of the value of the corresponding rate constant at any temperature. The determination of the rate constant involves an accurate experimental determination of both $A$ and $E$.

The results in Table 1 show clearly the effect of chemical structure. As far as the paraffins

[1] Steacie, "Atomic and Free Radical Reactions," Reinhold Pub. Corp., New York, 1954.
[2] Trotman-Dickenson and Steacie, *J. Chem. Phys.*, 1951, **19**, 329.
[3] Whittle and Steacie, *ibid.*, 1953, **21**, 993.

are concerned, it is evident that the activation energy for the removal of a hydrogen atom from a primary carbon atom is greater than that for secondary, which in turn is greater than that for a tertiary carbon atom. Unfortunately, errors in $E$ and $P$ compensate each other and it is difficult to get sufficient accuracy to make a detailed treatment of structure significant. The values of the absolute rates at a given temperature, shown in col. 3 of the Table, are much more reliable. It will be seen that there is the same trend, hydrogen atoms attached to tertiary atoms being the most reactive, followed by those on secondary and then primary as would be expected from chemical evidence.

A surprisingly good correlation is obtained if one takes the rate constant " per active H-atom." Thus for ethane there are six hydrogen atoms on primary carbon atoms. If the value in col. 3 is divided by 6 we obtain $0{\cdot}6 \times 10^{13}$ as the value of $k_{1a}/k_2^{\frac{1}{2}} \times 10^{13}$ at 182° c. In a similar way for 2 : 2-dimethylpropane, with 12 hydrogen atoms on primary carbon atoms, and 2 : 2 : 3 : 3-tetramethylbutane with 18, we obtain 0·5 and $0{\cdot}6 \times 10^{13}$. The values in the last column show very striking differences between hydrogen atoms on primary, secondary, and tertiary carbon atoms.

In the case of the olefins a similar correlation is obtained if we consider the nature and number of the hydrogen atoms in an α-position to the double bond. Here again the order of reactivity is tertiary > secondary > primary.

The cyclic hydrocarbons again yield results in line with the chemical evidence. The rates of abstraction from *cyclo*pentane and *cyclo*hexane, where there is little strain in the ring, are almost exactly the same as that for a secondary hydrogen in a paraffin.

Again, as expected, toluene is much more reactive than benzene. Actually, however, the difference is perhaps less than one might expect in view of the frequently assumed great difference in bond dissociation energies between the ring and side-chain hydrogen atoms.

*Other Radical Sources.*—A considerable number of investigations have been made in which other sources of methyl radicals have been used from which it is possible to get similar information about reactions of the type $CH_3 + RH \longrightarrow CH_4 + R$. This furnishes a very valuable check on the results given in Table 1. A number of such results are given in Table 2. It is

TABLE 2. *Results with various sources of methyl radicals.*[1]

| Reactant | Radical source | $E$ (kcal.) | $k$ at 182° c. $\times 10^{-4}$ (mole$^{-\frac{1}{2}}$ cm.$^{\frac{3}{2}}$ sec.$^{-1}$) |
|---|---|---|---|
| 2-Methylpropane | Acetone | 7·6 ± 0·2 | 22 |
| | $Hg(CH_3)_2$ | 7·3 ± 0·3 | 16 |
| | Azomethane | 6·7 ± 0·3 | 10 |
| Toluene | Acetone | 8·3 ± 0·3 | 14 |
| | $Hg(CH_3)_2$ | 7 ± 2 | 5 |
| | DTBP • | 11 ± 2 | — |
| Methanol | Acetone | 8·2 ± 0·2 | 6 |
| | $Hg(CH_3)_2$ | 8·2 ± 0·5 | 5 |
| Ethyleneimine | DTBP • | 4·8 ± 0·3 | 260 |
| Azomethane | Azomethane | 7·6 | ~20 |
| Dimethyl ether | Acetone | 9·5 ± 0·2 | 9 |
| | $Hg(CH_3)_2$ | 8·4 ± 1·5 | 9 |
| | $CH_3{\cdot}O{\cdot}CH_3$ | 10 ± 2 | 12 |
| *n*-Butane | Acetone | 8·3 ± 0·2 | 11 |
| | $Hg(CH_3)_2$ | 8·2 ± 0·5 | 22 |
| | $Hg(CH_3)_2$ | 9·5 ± 0·5 | 10 |
| | $Hg(CH_3)_2$ | — | 13 |
| | Azomethane | 9·1 ± 0·3 | — |
| *cyclo*Propane | Acetone | 10·3 ± 0·4 | 1·1 |
| | $Hg(CH_3)_2$ | 10·2 ± 1·0 | 1·5 |
| Ethylene oxide | $Hg(CH_3)_2$ | 9·0 ± 1·0 | 1·5 |
| | $Hg(CH_3)_2$ | 9·6 ± 2 | 2·8 |
| Acetaldehyde | DTBP • | 8·0 ± 0·3 | 220 |
| Acetone | Acetone | 9·7 ± 0·1 | 10 |
| | Acetone | 9·6 ± 0·4 | 8 |
| | Acetone | 9·5 ± 0·2 | 11 |
| | DTBP • | 9·5 ± 1·0 | 9 |
| Diacetyl | Diacetyl | 7·1 ± 0·2 | 17 |
| Di-*tert*.-butyl peroxide | DTBP • | (15) | 2 |
| Dimethylmercury | $Hg(CH_3)_2$ | 9·0 ± 0·5 | 10 |
| | $Hg(CH_3)_2$ | 11·0 | 3 |
| Dimethylcadmium | $Cd(CH_3)_2$ | (14) | 2 |

• DTBP = Di-*tert*.-butyl peroxide.

evident that, in general, the agreement between different workers, using different sources of radicals, is excellent. In particular, the rate constants at a given temperature are almost always in agreement to within a factor of 1·5. This agreement indicates strongly that the results are not in error because of errors in mechanism, and there is no reason to suspect the participation of " hot " radicals.

*Isotope Effects.*—Since deuterium tracer methods have been largely used in the investigation of methyl-radical reactions, it is important to consider isotope effects. The more clear-cut case is the group of reactions of the type $CH_3 + H_2 \longrightarrow CH_4 + H$, and we will consider this as an example. The effects to be expected are not large compared with experimental errors, and since errors in $E$ and $A$ are compensating, it is difficult to obtain reliable results. We will therefore confine our attention to absolute values of rate constants at a given temperature, since these are much more accurate. Results are given in Table 3.

The main point which is evident from the Table is that reactions involving the breaking of the stronger D–D bond are considerably slower than those involving the H–H bond. On the other hand, there is relatively little difference between reactions of $CH_3$ and of $CD_3$.

*Higher Alkyl Radicals.*—There is not much information about the hydrogen-abstraction reactions of higher alkyl radicals. Since $D(C_2H_5{-}H)$ is 4—5 kcal. less than $D(CH_3{-}H)$, hydrogen abstraction by ethyl radicals will be 4—5 kcal. less exothermic than the corresponding reactions with methyl radicals. This might be expected to be reflected in higher activation energies. Table 4 gives most of the relatively few data which are available.

TABLE 3. *Reaction of methyl radicals with hydrogen isotopes.*

(Whittle and Steacie.[3])

| Reaction | $k_A/k_B^{\frac{1}{2}} \times 10^{12}$ * at 210° c. | Reaction | $k_A/k_B^{\frac{1}{2}} \times 10^{12}$ * at 210° c. |
|---|---|---|---|
| $CH_3 + D_2 \longrightarrow CH_3D + D$ ... | 7·85 | $CH_3 + HD \longrightarrow CH_4 + D$ ... | 9·1 |
| $CH_3 + H_2 \longrightarrow CH_4 + H$ ... | 22·0 | $CH_3 + HD \longrightarrow CH_3D + H$ | 5·1 |
| $CD_3 + H_2 \longrightarrow CD_3H + H$ ... | 26·5 | $CD_3 + HD \longrightarrow CD_3H + D$ | 10·4 |
| $CD_3 + D_2 \longrightarrow CD_4 + D$ ..... | 8·9 | $CD_3 + HD \longrightarrow CD_4 + H$ ... | 6·0 |

* $k_A$ is the rate constant of the hydrogen-abstraction reaction, $k_B$ that of the recombination of methyl radicals.

TABLE 4. *Hydrogen-abstraction by ethyl radicals.*

| Substance | $E$ (kcal.) | $P$ (approx.) | Ref. | Substance | $E$ (kcal.) | $P$ (approx.) | Ref. |
|---|---|---|---|---|---|---|---|
| $Hg(C_2H_5)_2$ ..... | 6·2 | $1 \times 10^{-4}$ | 4 | $D_2$ ..... | 13·4 | $10^{-3}$ | 6 |
| $CO(C_2H_5)_2$ ..... | 7·4 | $3 \times 10^{-4}$ | 5 | $C_2H_5{\cdot}N{:}N{\cdot}C_2H_5$ ... | 7·4 | $10^{-3}$ | 7 |
| $CH_3{\cdot}CO{\cdot}C_2H_5$ ..... | 8·0 | $1 \times 10^{-4}$ | 8 | | | | |

Few data exist on hydrogen abstraction by radicals higher than ethyl. The abstraction of hydrogen from azo*iso*propane by *iso*propyl radicals [9] and that from di-*n*-propyl ketone by *n*-propyl radicals [10] both have activation energies of about 6·5 kcal. The reaction $Pr^i + H_2 \longrightarrow C_3H_8 + H$ has an activation energy of about 12·5 kcal.[11]

It appears, therefore, that there is on the whole not much difference in reactivity between methyl, ethyl, and propyl radicals in spite of the difference in heats of reaction. This emphasizes the danger of assuming a parallelism between heats of reaction and activation energies. An extreme case of the absence of such a parallelism is the series of reactions

$$CH_3 + CH_4 \longrightarrow CH_4 + CH_3 \qquad CH_3 + H_2 \longrightarrow CH_4 + H \qquad CH_3 + HCl \longrightarrow CH_4 + Cl$$

The bond dissociation energies of $CH_4$, $H_2$, and HCl are all identical to within $\pm 1$ kcal., but the activation energies are respectively about 12, 10, and 5 kcal.

*Reactions of Trifluoromethyl Radicals.*—Some recent work by Ayscough has given interesting results on the reactions of $CF_3$ radicals. If hexafluoroacetone is photolysed the mechanism is,

[4] Ivin and Steacie, *Proc. Roy. Soc.*, 1951, *A*, **208**, 25.
[5] Kutschke, Wijnen, and Steacie, *J. Amer. Chem. Soc.*, 1952, **74**, 714.
[6] Wijnen and Steacie, *J. Chem. Phys.*, 1952, **20**, 205.
[7] Ausloos and Steacie, *Bull. Soc. chim. belges*, 1954, **63**, 87.
[8] *Idem, Canad. J. Chem.*, 1955, **33**, 1062.
[9] Durham and Steacie, *ibid.*, 1953, **31**, 377.
[10] Masson, *J. Amer. Chem. Soc.*, 1952, **74**, 4731.
[11] Hoey and LeRoy, *Canadian J. Chem.*, 1955, **33**, 580.

deactivation of excited molecules being neglected, *i.e.*, only those molecules which decompose being considered:

$$CF_3{\cdot}CO{\cdot}CF_3 + h\nu \longrightarrow 2CF_3 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (21)$$

$$2CF_3 \longrightarrow C_2F_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (22)$$

The reaction is thus extraordinarily simple. The simplicity by comparison with the decomposition of ordinary acetone appears to arise from two facts. In the first place, $CF_3{\cdot}CO$ is too unstable to be a complication. Secondly, because of the very strong C–F bonds, the reaction

$$CF_3 + CF_3{\cdot}CO{\cdot}CF_3 \longrightarrow CF_4 + CF_2{\cdot}CO{\cdot}CF_3$$

does not appear to occur, at least at temperatures up to 120° c. If now a hydrocarbon RH is added, the reactions

$$CF_3 + RH \longrightarrow CF_3H + R \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (23)$$

$$CF_3 + R \longrightarrow CF_3R \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (24)$$

$$2R \longrightarrow R_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (25)$$

will occur. A determination of $CF_3H$ and $C_2F_6$ then enables us to make use of the relations $R_{C_2F_6} = k_{22}[CF_3]^2$ and $R_{CF_3H} = k_{23}[CF_3][RH]$, and hence

$$k_{23}/k_{22}^{\frac{1}{2}} = R_{CF_3H}/(R_{C_2F_6}^{\frac{1}{2}}[RH])$$

It is thus possible to determine values of $k_{23}/k_{22}^{\frac{1}{2}}$ for a series of hydrocarbons, RH. Since Ayscough has made a direct determination of $k_{22}$, the rate constant for the recombination of radicals, by a sector method,[12] it is possible to calculate absolute values of $k_{23}$ at various temperatures. Actually, the rate of recombination of $CF_3$ radicals is very little different from that of $CH_3$ radicals. In Table 5 the results for $CF_3$ reactions are compared with those for $CH_3$ for a number of hydrocarbons. Some very recent results obtained by Pritchard, Pritchard, and Trotman-Dickenson [12a] are in excellent agreement with the values in Table 5.

In spite of certain discrepancies in the values for $CH_3$, there is no question that $CF_3$ reacts with a lower activation energy and much more rapidly than does $CH_3$.

All in all, the general state of our knowledge regarding metathetical reactions of this type appears to be fairly satisfactory, but more information is badly needed on the reactions of complex radicals.

TABLE 5. *Rate of reactions of the type* $CF_3 + RH \longrightarrow CF_3H + R$.[13]

| Reaction | $k_A/k_R^{\frac{1}{2}} \times 10^{13}$ * at 400° K. (cm.$^{3/2}$ mol.$^{-\frac{1}{2}}$ sec.$^{-\frac{1}{2}}$) | $P_A/P_R^{\frac{1}{2}}$ (400° K.) | $E_A$ (kcal.) | $k_A \times 10^{13}$ at 400° K. (cm.$^3$ mol.$^{-1}$ sec.$^{-1}$) |
|---|---|---|---|---|
| $CH_3 + CH_4$ | 0·029 | $6 \times 10^{-4}$ | 13—14 | 0·017 |
| $+ C_2H_6$ | 0·83 | $3 \times 10^{-4}$ | 10·4 | 0·49 |
| $+ C_3H_8$ | — | — | — | — |
| $+ n\text{-}C_4H_{10}$ | 5·8 | $3 \times 10^{-4}$ | 8·3 | 3·42 |
| $+ iso\text{-}C_4H_{10}$ | 12·6 | $3 \times 10^{-4}$ | 7·6 | 7·43 |
| $CF_3 + CH_4$ | 3·5 | $6 \times 10^{-3}$ | 10·3 | 2·19 |
| $+ C_2H_6$ | 104 | $6 \times 10^{-3}$ | 7·5 | 65 |
| $+ C_3H_8$ | 418 | $6 \times 10^{-3}$ | 6·5 | 261 |
| $+ n\text{-}C_4H_{10}$ | 631 | $2 \times 10^{-3}$ | 5·1 | 395 |
| $+ iso\text{-}C_4H_{10}$ | 1010 | $2 \times 10^{-3}$ | 4·7 | 631 |

* $k_A$ refers to the abstraction reaction and $k_R$ to the radical-recombination reaction in each case.

*Recombination and disproportionation of radicals.*

Another type of reaction to which I should like to give some attention is that involving the interaction of two radicals, *i.e.*, recombination and disproportionation. It is only within the last five or six years that any quantitative information has been available about this type of process, but the present situation appears to be fairly satisfactory.

In considering the recombination of free radicals two factors are concerned. One of these

[12] Ayscough, *J. Chem. Phys.*, 1956, **24**, 944.

[12a] Pritchard, Pritchard, and Trotman-Dickenson, *Chem. and Ind.*, 1955, 564.

[13] Ayscough, Polanyi, and Steacie, *Canad. J. Chem.*, 1955, **33**, 743; Ayscough and Steacie, *ibid.*, 1956, **34**, 103.

is the well-known third-body restriction on recombination reactions. This may be expected to hold stringently for the recombination of two atoms, and to be of little importance in the case of the recombination of two complex radicals which have many internal degrees of freedom to take care of the excess of energy. In the second place we may expect true steric factors to cut down the efficiency of the recombination for very complex radicals. It is therefore quite uncertain *a priori* what the efficiency will be for intermediate cases such as the recombination of methyl and ethyl radicals.

In considering the mechanism of recombination, one method is to treat the reaction as bimolecular ($2CH_3 \longrightarrow C_2H_6$), with an efficiency which varies with pressure. A more detailed mechanism involves the formation of a complex and its dissociation or stabilization, *i.e.*,

$$2CH_3 \longrightarrow C_2H_6^*$$
$$C_2H_6^* \longrightarrow 2CH_3$$
$$C_2H_6^* + M \longrightarrow C_2H_6 + M$$

where M is any third body. Recombination is, of course, merely the reverse of unimolecular dissociation. For the moment we will consider the process as a straight bimolecular reaction, and see what the collision efficiency is at ordinary pressures. Later we will come back to the effect of pressure.

In the case of methyl radicals three methods of investigation have been used. The first is to compare the rate of the reaction $CH_3 + CH_3 \longrightarrow C_2H_6$ with that of some other known reaction of methyl, in this case $CH_3 + NO \longrightarrow (CH_3{\cdot}NO)$. The rate of the latter reaction is known from experiments of the Paneth mirror-removal type. A second method involves the use of a mass-spectrometer to follow the decay of the methyl-radical concentration directly. The third method is the well-known intermittent light, or sector, method which has been widely used to determine radical lifetimes in polymer chemistry. This is by far the simplest and most accurate method. The first two methods give results which are in every way compatible with the sector method, and we will limit further discussion to the last method.

*The Sector Method.*—This method has been widely used, and I will not discuss the general theory here. There are, however, certain differences in its application, since we are not dealing with a chain reaction in the present case. The use of the sector method depends on the fact that the rate of a photochemical reaction with intermittent light is different from that with continuous illumination of the same total intensity. Such a condition will exist whenever the rate of the reaction is proportional to a power of the light intensity other than the first.

It is easy to see why this is the case. Suppose that methyl radicals are being produced photochemically; then the concentration of radicals will be greater the higher the intensity. Suppose now that they disappear from the system by two reactions and that the rates are

$$R_1 \propto [CH_3]$$
$$R_2 \propto [CH_3]^2$$

At high light intensities $R_2$ will gain on $R_1$. Hence $R_1$ will increase by a power of the intensity less than unity. (Actually in this case $R_1 \propto I^{\frac{1}{2}}$.)

Suppose that we consider the simplest possible case which might be used to measure the rate of recombination,

$$X + h\nu \longrightarrow 2CH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$
$$CH_3 + CH_3 \longrightarrow C_2H_6 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

If we could measure the stationary concentration of methyl radicals, then $k_2$ would follow immediately, since in the steady state

$$d[CH_3]/dt = 0 = 2I - k_2[CH_3]^2$$

Unfortunately, we can only measure the rate of production of stable products. In these circumstances the method will not work, since from the above we have

$$[CH_3] = (2I/k_2)^{\frac{1}{2}}$$
$$d[C_2H_6]/dt = k_2[CH_3]^2 = k_2 . 2I/k_2 = 2I$$

Hence every $CH_3$ formed gives $C_2H_6$ eventually, and the rate is proportional to $I$, not to $I^{\frac{1}{2}}$.

Gomer and Kistiakowsky,[14] who first investigated the methyl recombination by a sector method, got round the difficulty by using a pilot reaction as a competitor for $CH_3$. Thus, suppose we have

$$CH_3 + X \longrightarrow CH_4 + Y \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

One can then treat the system very simply by adjusting conditions so that (3) occurs only to the extent of 2 or 3% as compared with (2). In these circumstances $[CH_3]$ is not greatly affected by (3), and we still have

$$[CH_3] \sim (2I/k_2)^{\frac{1}{2}}$$

Hence $$d[CH_4]/dt = k_3[X][CH_3] = k_3[X](2I/k_2)^{\frac{1}{2}}$$

*i.e.*, the rate of production of $CH_4$ is proportional to $I^{\frac{1}{2}}$ and the sector method can be applied by following the rate of formation of $CH_4$ as a function of sector speed. (Actually, it is not necesary to use the above approximation, as the theory for the complete mechanism has been worked out in practical form by Kutschke and Dainton, Burnett and Wright, and Shepp.[14a])

Gomer and Kistiakowsky produced methyl radicals by the photolysis of dimethylmercury and of acetone, and used as " pilot reactions " the hydrogen-abstraction reactions

$$CH_3 + CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow CH_4 + CH_2{\cdot}CO{\cdot}CH_3$$

or $$CH_3 + Hg(CH_3)_2 \longrightarrow CH_4 + CH_2{\cdot}Hg{\cdot}CH_3$$

In this way they found the values given in Table 6.

TABLE 6.

(Pressure = 10—50 mm.)

| Radical source | Temp. (°c.) | $k_3$ (cm.$^3$ mole$^{-1}$ sec.$^{-1}$) | Radical source | Temp. (°c.) | $k_3$ (cm.$^3$ mole$^{-1}$ sec.$^{-1}$) |
|---|---|---|---|---|---|
| Acetone ..... | 125° | $4{\cdot}5 \times 10^{13}$ | Dimethylmercury | 175° | $4{\cdot}6 \times 10^{13}$ |
| Acetone ..... | 175 | $4{\cdot}2 \times 10^{13}$ | Dimethylmercury | 250 | $6{\cdot}7 \times 10^{13}$ |

The rate constants correspond to recombination at approximately every collision of two methyl radicals.

*The Effect of Pressure on the Recombination of Methyl Radicals.*—Two investigations have been made recently, by Kistiakowsky and Roberts [15] and by Dodd and Steacie,[16] in which the effect of pressure on the recombination has been studied in detail by photolysing acetone at low pressures. Kistiakowsky and Roberts extended the experiments of Gomer and Kistiakowsky. At a pressure of 10 mm. the rate constant for the recombination of methyl radicals was found to be $3{\cdot}7 \times 10^{13}$ cm.$^3$ mole$^{-1}$ sec.$^{-1}$, corresponding to a collision efficiency of about unity. There is thus good agreement with Gomer's work. The rate constants decreased with pressure down to 1 mm., the lowest pressure studied. The decrease in rate was in agreement with a mechanism in which the rate becomes dependent on the stabilization of an excited complex by collision with a third body. Thus for the mechanism we may write

$$CH_3{\cdot}CO{\cdot}CH_3 + h\nu \longrightarrow 2CH_3 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$CH_3 + CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow CH_4 + CH_2{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$CH_3 + CH_3 \longrightarrow C_2H_6^* \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$C_2H_6^* \longrightarrow 2CH_3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$C_2H_6^* + CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow C_2H_6 + CH_2{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Their results fit such a mechanism excellently and indicate a decrease of a factor of 3 to 4 in the recombination rate constant over the pressure range 10—1 mm.

[14] Gomer and Kistiakowsky, *J. Chem. Phys.*, 1951, **19**, 85.
[14a] Kutschke, James, and Dainton, unpublished work; Burnett and Wright, *Proc. Roy. Soc.*, 1954, *A*, **221**, 37; Shepp, *J. Chem. Phys.*, 1956, **24**, 939.
[15] Kistiakowsky and Roberts, *ibid.*, 1953, **21**, 1637.
[16] Dodd and Steacie, *Proc. Roy. Soc.*, 1954, *A*, **223**, 283.

Dodd and Steacie investigated the acetone photolysis with steady illumination down to a presssure of about 0·1 mm., and inferred the fall in the rate of recombination at lower pressures from the changing value of the ratio $k_5/k_2^{\frac{1}{2}}$.

The results of both investigations may be treated in the following way. If it is assumed that in the acetone photolysis methane comes only from reaction (5) and ethane from (2), then for second-order recombination

$$\rho = \frac{k_5}{k_2^{\frac{1}{2}}} = \frac{R_{CH_4}}{R_{C_2H_6}^{\frac{1}{2}}[CH_3{\cdot}CO{\cdot}CH_3]}$$

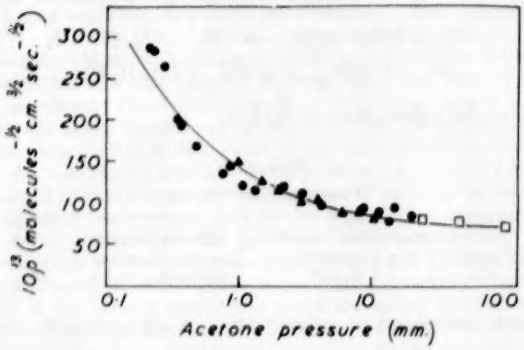
If recombination occurs by a third-order process

$$2CH_3 + CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow C_2H_6 + CH_3{\cdot}CO{\cdot}CH_3 \quad . \quad . \quad . \quad . \quad (9)$$

then

$$r = \frac{k_5}{k_9^{\frac{1}{2}}} = \frac{R_{CH_4}}{R_{C_2H_6}^{\frac{1}{2}}[CH_3{\cdot}CO{\cdot}CH_3]^{\frac{1}{2}}}$$

FIG. 1.




In the intermediate region, similarly,

$$\rho = \frac{k_5}{k_6^{\frac{1}{2}}}\left(\frac{k_5}{k_6[CH_3{\cdot}CO{\cdot}CH_3]} + 1\right)^{\frac{1}{2}}$$

and reduces to $k_5/k_6^{\frac{1}{2}}$ at high pressures. At lower pressures the ratio will rise. This is shown by Fig. 1.

Similarly, in the intermediate range

$$r = \frac{k_5}{k_6^{\frac{1}{2}}}\left(\frac{k_7}{k_8} + [CH_3{\cdot}CO{\cdot}CH_3]\right)^{\frac{1}{2}}$$

At low pressures this will reduce to a constant value. Fig. 2 shows the results plotted in this way. There is thus excellent agreement between all investigations and there seems to be no doubt that the recombination is becoming strongly pressure-dependent at low pressures. At the lowest pressures there is also some evidence of heterogeneity.

The effect of foreign gases on the recombination has also been investigated. Kistiakowsky and Roberts found that carbon dioxide was only about 1/40 as efficient as acetone as a third body. Dodd found the following approximate efficiencies relative to acetone :

| | | | |
|---|---|---|---|
| Argon | <0·03 | Benzene | 1·0 |
| Carbon dioxide | 0·03 | (Acetone) | (1·0) |
| Decafluorobutane | 0·2 | Acetaldehyde | 3·0 |
| Perfluoromethyl*cyclo*hexane | 0·3 | | |

*Ethyl Radicals.*—The reaction of two ethyl radicals is more complex than that of two methyls, since in addition to recombination to form butane, disproportionation to ethane and ethylene

FIG. 2.

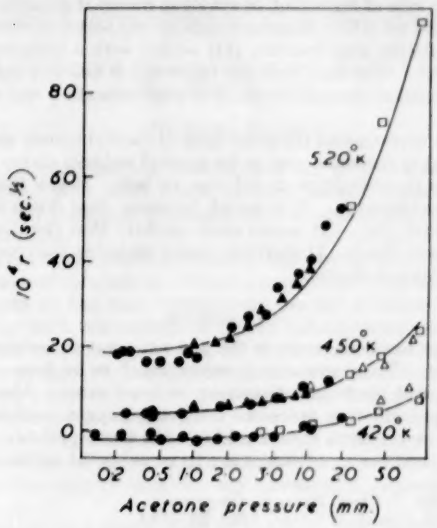
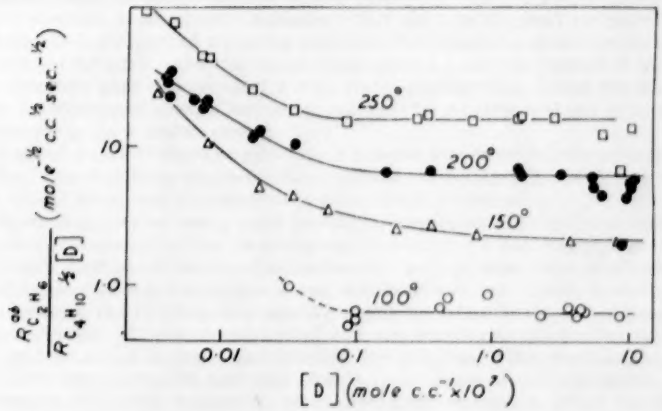



FIG. 3.




also occurs. The best investigated case is that of the diethyl ketone photolysis, the main steps in the mechanism of which are :[5]

$$C_2H_5{\cdot}CO{\cdot}C_2H_5 + h\nu \longrightarrow 2C_2H_5 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$2C_2H_5 \longrightarrow C_4H_{10} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$2C_2H_5 \longrightarrow C_2H_6 + C_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

$$C_2H_5 + C_2H_5{\cdot}CO{\cdot}C_2H_5 \longrightarrow C_2H_6 + C_2H_4{\cdot}CO{\cdot}C_2H_5 \quad . \quad . \quad . \quad . \quad (13)$$

$$C_2H_5 + C_2H_4{\cdot}CO{\cdot}C_2H_5 \longrightarrow C_4H_9{\cdot}CO{\cdot}C_2H_5 \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

$$2C_2H_4{\cdot}CO{\cdot}C_2H_5 \longrightarrow (C_2H_4{\cdot}CO{\cdot}C_2H_5)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

$$C_2H_4{\cdot}CO{\cdot}C_2H_5 \longrightarrow C_2H_4 + CO + C_2H_5 \quad . \quad . \quad . \quad . \quad . \quad (16)$$

Conditions can be adjusted so that reaction (16) is unimportant. In these circumstances the determination of the rate of formation of ethylene makes it possible to differentiate between ethane formed by (12) and by (13). Measurements by the sector method with diethylmercury [4] and diethyl ketone [17] indicate that reaction (11) occurs with a collision efficiency of the order of 0·1 at higher pressures. The fact that the efficiency is below 1 may be due merely to the uncertain meaning of collision cross-sections, or it may indicate a real steric effect for the more complex ethyl radicals.

Brinton has recently investigated the photolysis of diethyl ketone at low pressures.[18] Fig. 3 shows the results treated in the same way as for methyl radicals above. It will be seen that no third-body effects are noticeable down to 0·1 mm. or less. Below this pressure heterogeneous processes complicate the situation. It is found, however, that down to 0·01 mm. or less there is no change in the ratio $k_{13}/k_{11}$. It seems most unlikely that the disproportionation reaction (12) would show a pressure effect. It therefore seems probable that reaction (11) is independent of pressure down to at least 0·01 mm.

### *Conclusion.*

Considerable progress has been made in the last ten years in building up a chemistry of free radicals in the gas phase. There remains, however, much to be done. Our knowledge of bond dissociation energies is still far from satisfactory in most cases. Also there is much interest today in combustion and in other processes involving oxygen-containing radicals. This is a very difficult field, and as yet not a great deal has been accomplished. It is, however, a field of very great importance, and major advances are to be expected within the next few years.

[17] Shepp and Kutschke, *J. Chem. Phys.*, in the press.
[18] Brinton and Steacie, *Canad. J. Chem.*, 1955, **33**, 1840.

# *Personal Reminiscences of a Radiochemist.*

THE FARADAY LECTURE, DELIVERED BEFORE THE SOCIETY AT NOTTINGHAM ON MARCH 28TH, 1956.

By OTTO HAHN.

I CONSIDER it a great honour that you have invited me to give a lecture associated with the name of Michael Faraday. And when I look through the list of eminent scientists who have lectured in memory of that truly epoch-making chemist and physicist I would be ashamed to think of competing with them.

I have devoted a great many years to Science, but nearly all of them only to research on radium and other radioactive substances. What a narrow field this seems when compared with the gigantic achievements of the man whose work we are commemorating today, and very narrow too in comparison with the content of earlier Faraday lectures.

For the last ten years or more I have had no opportunity of doing any scientific research, so I have no new results of my own to submit to you. You have however very kindly allowed me to tell you something about my earlier work and it is with sincere gratitude that I avail myself of your permission to turn this Faraday Lecture into something more like a piece of personal history—a short survey of my former researches. It is also a source of peculiar gratification to me that at the close of my scientific life you have afforded me the opportunity of once more lecturing in the country in which my career as a radiochemist began, that is, in England.

It was in the autumn of 1904 that I came to London. The only asset I had was an introduction to Sir William Ramsay from Professor Zincke, the Professor in Marburg who had supervised my doctor thesis (on some branch of organic chemistry) and under whom I had subsequently worked for two years as assistant. Actually I had come to England to learn the language, because there was a prospect of my being appointed to a special post as organic chemist in the German chemical industry; and this would have entailed a certain amount of work abroad.

It was therefore pure chance—and a very lucky chance—that I had the good fortune to work under Sir William Ramsay; and it was followed by what turned out to be a whole series of lucky chances in my scientific career.

When I called on Sir William he asked me if I would like to work with radium. I told him that to date I knew nothing whatever about radium; whereupon he said that was no disadvantage, it would mean that I tackled the work without prejudice.

Sir William then handed me a bowl holding a considerable quantity of barium chloride, remarking that it contained about 10 milligrams of radium. I was to separate the radium by Madame Curie's method of fractional crystallization and produce from it a series of organic salts with the object of determining the atomic weight of radium. Owing to the high molecular weights of the salts, the 10 milligrams would possibly be sufficient for the purpose.

I started to work. I became acquainted with the transformation products of radium—its emanation and its active deposit—and checked the progress of the fractional crystallization. I obtained some strange results and very soon became aware of the appearance, side by side with the long-lived radium emanation, of a short-lived emanation which turned out to be thorium emanation. As the emanation was much more intense than that derived from thorium salts of equal weight, I was obliged to conclude that my preparations contained a new radio-element—the parent substance of this thorium emanation. I called the new element radiothorium. The explanation lay in the fact that the radium preparation which had been handed to me had been extracted from a mineral which contained both thorium and uranium. The discovery of radiothorium was therefore purely accidental.

Ramsay was interested in this result and helped me, particularly in the matter of my lack of space. I was desperately in need of some place to carry out my measurements, as Sir William Ramsay's laboratories at the Institute were very overcrowded. After a while he gave me a master-key which enabled me to enter the Chemical Institute and the neighbouring Physics Institute at night and carry out my measurements in one of its ante-rooms.

When my stay in London was drawing to a close, Sir William asked me what my future plans were. I told him that I intended to go into chemical industry. He suggested however that I should continue working on radioactivity and try for a Readership at the University of Berlin with a dissertation on this new subject. Following up that idea, Sir William wrote a

letter to his friend Emil Fischer, the Director of the Berlin Chemical Institute, and Fischer replied that he was willing to take me.

This decided me to continue on the path of radium research, but I was nervous because I still knew so little about the subject. So in the summer of 1905 I wrote to Professor Ernest Rutherford in Montreal and asked him whether I might work under him for a time, that I had discovered a new radioactive element and was anxious to learn more about the subject. Rutherford sent me a very friendly answer; but he did not mention radiothorium.

When I joined him in Montreal in 1905 he questioned me about the new radio-element, but I noticed a certain reserve in his manner. After a few days he admitted to me that he had not believed in radiothorium, the discovery of which I had already briefly published. Later I heard that the eminent radiochemist B. B. Boltwood, a friend of Rutherford's, had written to him about radiothorium in a letter which contained the sentence: "The radiothorium discovered by Hahn seems to be a mixture of thorium X and stupidity." However, Boltwood was soon convinced. But the half-life value of the new substance became a subject of controversy. I had reported that the radiothorium disintegrates with a half-life period of about two years. Boltwood's thorium salts, however, showed too little activity (they did not contain the equilibrium amount of radiothorium) and this did not increase in accord with the 2 years' half-life. So my determination seemed to be wrong. When discussing the matter with him, I set up the hypothesis that it might be possible to explain our differing results by means of a longer-lived non-radiating substance between thorium and radiothorium, one which was not contained in his weak thorium salts and would be produced later.

After my return to Germany, I found that hypothetical substance; I called it mesothorium. Incidentally, the discussion which Boltwood and I had had on the subject led to a close friendship which lasted till his early death. When I wrote to him about mesothorium he congratulated me and pointed out that my hypothesis had proved correct after all.

While in Montreal, I found a new product in actinium—an intermediary substance between actinium itself and actinium X, which had been discovered under Rutherford; I called it radioactinium. It had been overlooked in Montreal and so I had my own little triumph to compensate for their disbelief in my radiothorium. In that first decade of radium research it was still very easy to discover new radio-elements.

Together with Rutherford I investigated the range of the $\alpha$-rays emitted by radiothorium and its $\alpha$-radiating transformation products, confirming that $\alpha$-rays emitted by uniform substances have a uniform range. In the course of these researches I also found a very short-lived transformation product of the active deposit; today this is known as thorium C'.

While working with thorium preparations which led to the discovery of mesothorium in Berlin, I was supplied with very pure thorium salts. In these I found, besides the short-lived thorium emanation, very minute traces of radium emanation which increased linearly with the time. From this it was easy to deduce that the thorium contained traces of radium's parent substance, which had long been searched for, and that chemically it must be very like thorium. I started to look for this substance in the "hydroxides" group obtained in the process of extraction of radium from pitchblende. These hydroxides had to contain the thorium-like substance. But before I obtained a sample of these hydroxides from Austria, Boltwood published his discovery of ionium, radium's long-lived parent substance. This time Boltwood was ahead of me.

Boltwood too stressed the similarity between his ionium and thorium—a similarity already indicated by my observations in connection with the pure thorium salts.

About that time my attention was drawn to certain other great chemical similarities. Despite numerous attempts I was unable to separate mesothorium from radium and I very soon realized that the radiothorium in Ramsay's radium–barium salt had been generated from the mesothorium which had come down together with the radium. As mesothorium could not be separated from radium and as it did not emit any perceptible rays, I had been unable to find it earlier.

A similar lack of success having attended my efforts to separate radiothorium from thorium, it was a logical conclusion that these elements too must be chemically very much alike. But I lacked the courage to conclude that the chemical properties of, for instance, radium, mesothorium, and thorium X, or of thorium, ionium, and radiothorium were genuinely identical. Frederick Soddy, a few years later, was the first to realize that certain elements exist which have identical chemical properties and occupy the same position in the Periodic Table, but whose atomic weights differ. He called them isotopic elements. Thus, with Soddy's discovery of isotopes, all the difficulties in the way of classifying the various radio-elements vanished at

one blow. Since that time we no longer speak of inseparable elements, but of isotopic atoms of one and the same element.

In the autumn of 1907 Dr. Lise Meitner, a young physicist, came from Vienna to Berlin to improve her theoretical physics under Max Planck, and also to continue the work on radioactivity that she had begun in Vienna. She came to me, and out of that visit to Berlin there grew up our collaboration and a friendship which has lasted for over thirty years.

At that time I already had quite a number of different radioactive preparations, and so Lise Meitner and I began a systematic study of the β-rays emitted by these substances. We drew up exact absorption curves, believing that uniform radio-elements would emit uniform β-rays, that is, rays of identical velocity. Working on this hypothesis we actually did find β-rays emitted by elements which till then had been considered to be non-radiating.

But when we examined the rays from very thin foils of the matter in a magnetic field—just as Rutherford had done earlier with the α-particles—it became evident that our hypothesis was wrong. We obtained line spectra, and the rays were anything but uniform. In the long run, however, work on the magnetic β-spectra led to most important results, mainly obtained by Lise Meitner and her co-workers, particularly in connection with the part played by β- and γ-rays in atomic disintegration.

To return to chemistry: I should now like to show by an example how quite unspectacular observations can often lead to interesting results.

In 1907 the Vienna Radium Institute published an article on a very slight activity observed in the active deposit of actinium, for which no explanation could be found. Could there be traces of a new radio-element? On examination I found that the activity was caused by very small quantities of actinium X, the parent-substance of actinium emanation. But how did this definitely non-volatile alkaline-earth metal get into the active deposit? The explanation was found by means of the following observations: Thin foils of radioactinium, the parent substance of actinium X, and equally thin foils of actinium X itself, were compared. Residual activity was found in the active deposit when the radioactinium was used, but was not found at all in the case of actinium X. It followed that the α-particles of the radioactinium were responsible for the remaining activity. The α-particles of the radioactinium cause a "recoil" of the decay product actinium X, part of which may be ejected from the preparation; in consequence, minute traces can be found outside.

A short time later Lise Meitner and I, using this new "recoil" method, had discovered some new short-lived transformation products from α-radiating precipitates. Today the recoil method is widely used in nuclear physics to separate active disintegration products. The recoil of a radioactive disintegration may lead, not only to a physical separation, but also to the breaking of chemical bonds; such a procedure is now frequently applied in the concentration of artificial radio-elements and known under the name of the Szilard–Chalmers process.

Another observation, which was at first erroneously interpreted, later led to a method used in applied radiochemistry which I called the "emanation" method.

It depends on radium and thorium emanations from precipitates which contain traces of the emanating radio-elements.

Numerous radiochemical studies were undertaken with this "emanation" method: systematic surface changes under thermal treatment; lattice transformations of crystalline substances, where the transformation is recognizable by a momentary outburst of the emanation; disintegration temperatures; and reactions in the solid state—all these can be examined by the "emanation" method. Later, Dr. Strassmann and I used this method during our work on "fission" of uranium to obtain short-lived products from xenon and krypton given off during fission by uranium preparations of very high surface area.

Once Frederick Soddy had discovered isotopes and the Rutherford–Bohr model of the atom had been set up, the system of our chemical elements became clear for all to see.

But up to the year 1917, one active element was still missing, namely the parent substance of actinium. It had to be an element with the nuclear charge 91. Indeed an isotope of this element was found by Fajans and Göhring which disintegrated in a very few minutes and which they called brevium; today it is called $UX_2$. But despite intensive search Fajans and Göhring did not discover the parent substance of actinium. It was found simultaneously and independently by Dr. Meitner and myself and by Soddy and Cranston. We named it protactinium. Its isolation in a pure form was first achieved by my co-worker, A. von Grosse. Later we produced several hundred milligrams of this element in the form of a double fluoride. Protactinium has a half-life of 32,000 years and can therefore be extracted by the gram from uranium

minerals. The name protactinium has since been generally adopted for this long-lived form of the element 91.

In connection with element 91 I should like to give another example, this time again to show that it is important to follow up even infinitesimal inconsistencies when investigating radiochemical phenomena. Thirty years ago I noticed in the filtrate of a uranium X precipitate that its decay was not proceeding quite as one would have expected. The filtrate should have contained only the short-lived uranium X2. But in one preparation of the filtrate, I found, surprisingly, a just detectable residual activity which decreased rather too slowly. Repeating the experiment with stronger preparations, I discovered traces of the presence of an unknown radio-element with a 6·7-hour half-life; its activity was only about one-thousandth of that of uranium X and was therefore not easy to detect. It looked as if the unknown substance were a member of a hitherto undiscovered radioactive disintegration series, and I therefore tried to find the parent substance of this new body which I called uranium Z.

But these experiments led to no result and it became evident that uranium Z, like uranium X2, known much earlier, was derived from the well-known uranium X1, that is, they both had the same parent substance. In itself this was not a very spectacular result; but it happened to be the first case in which "isomerism" had been definitely proved in the course of a radioactive transformation. The next cases of nuclear isomerism were not found until twenty years later. Today they play an increasingly important part in atomic physics.

Other radiochemical investigations which we undertook at that time were of value for our later research on uranium. I refer to the detailed observations we made on the separation of minute quantities of radioactive substances with weighable amounts of precipitates. We investigated systematically the difference between the mixed-crystal type in the lattice and the adsorption of infinitesimal quantities which depended on precipitation conditions. Following experiments by Paneth and by Fajans, we formulated rules for precipitation and adsorption which clarified the behaviour of minute quantities of radioactive substances under the various conditions of precipitation. As a secondary result we found an explanation for the strange presence of helium in certain potassium salts occurring in Nature when other potassium salts from the same source contain no helium.

The discovery of protactinium, element 91, filled the last gap in the three great transformation series of the natural radio-elements.

In the early twenties, however, a new "age of nuclear research" set in. It was introduced by the first *artificial* transformation of one element into another due to the genius of Ernest Rutherford; when nitrogen nuclei were bombarded with helium nuclei, that is α-particles, the nitrogen nuclei were converted into oxygen and hydrogen. Artificial transmutation of the elements had become an accomplished fact. At first, it is true, this had only been achieved for infinitesimally minute quantities, and there was no hope that the discovery could be further exploited.

Then, in the early thirties, came the discovery of the neutron by James Chadwick, and in 1934 M. and Mme. Joliot-Curie discovered artificial radioactivity.

The discovery of the neutron meant that there was a simple explanation for isotopic phenomena. Chemical elements are composed of protons and neutrons. The number of protons determines the atomic number, that is, the chemical nature of the element. The sum of the protons and the neutrons gives the atomic weight.

In the course of atomic nuclear research it was soon realized that the uncharged neutrons are a peculiarly suitable munition for achieving atomic transformations; and it was the Italian scientist Enrico Fermi who pointed out the great importance of neutrons for nuclear transformations. He and his co-workers bombarded almost all the elements in the whole Periodic Table and produced numerous artificial radioactive isotopes. In general, the process consists in the neutron's being taken up by the nucleus; but the newly formed isotope is unstable and, emitting β-rays, is converted into the next higher element.

Fermi had carried out these experiments up to uranium and here too had found two very rapid transformations with β-ray emission. Quite logically he concluded that with uranium the process was the same as with the lower elements, and that therefore isotopes of the next higher element, that is, of element 93, had been produced from uranium, element 92.

Fermi's conclusions, however, were criticized by others. It was suggested that a 13-minute body found by Fermi might be an isotope of the next lower element 91, that is, an isotope of protactinium. As Dr. Meitner and I had found protactinium twenty years earlier and were acquainted with its chemical properties, and as moreover I had discovered uranium Z, the

β-ray emitting isotope of protactinium that disintegrates in about 6 hours, we felt authorized to check Fermi's experiments. We bombarded uranium with a neutron-producing radium–beryllium preparation, added uranium Z to the solution, and with that indicator for element 91 we examined the chemical properties of Fermi's 13-minute body. The result left in us no shadow of a doubt: Fermi's discovery was certainly not element 91, so his conclusion that it was an isotope of element 93 must be correct.

It should be pointed out that at that time no other possibility was to be thought of. A large number of nuclear reactions had been demonstrated with the help of artificial radiation sources and with the neutron. The resulting products were always isotopes of the bombarded element or of its nearest neighbours in the Periodic Table. It was considered impossible that there could be any different reaction.

Together with Fritz Strassmann, Professor Meitner and I continued the experiments on the bombardment of uranium which had been begun by Fermi, because the processes turned out to be much more complicated than was at first suspected. In the course of several years we isolated a large number of artificially active atoms which developed from each other under β-radiation and were therefore taken to be transuranic elements with rising atomic numbers. We believed we had reached element 96. In so far as our experimental work was repeated in other research institutes, these results were fully confirmed.

In July 1938, Lise Meitner had to leave Germany because of Hitler's racial laws; our collaboration came to an enforced end, but our friendship endures to this day. Strassmann and I continued the experiments and, while checking some new work of Mme. Joliot-Curie and Savitch, in the autumn of 1938 we again reached some very curious results. Apart from the numerous substances which were considered to be transuranic, we found a new group of artificial atoms which, we assumed, were artificial radium isotopes. Our conclusion was inescapable insofar as the chemical properties of these substances limited the possibilities only to radium or to the barium which had been used as separator. Barium was excluded by the rules of physics as they then stood—the physicists refused even to discuss any other possibility. Therefore only radium remained.

As became clear later we were very fortunate in having only very weak preparations at our disposal. In order to measure our preparations more accurately, we had to use thinner films, particularly for a long-lived isotope with a half-life period of 300 hours with very absorbable β-rays. Therefore we had to try to separate this 300-hour substance from barium. As is well-known, this is done by fractional crystallization, a process with which we had been familiar for many years; in particular, I had used it for the concentration of the radium isotope, mesothorium, from barium. But all our experiments failed; our radium did not increase in the first crystallizations. It seemed plausible to attribute this failure to the extremely low activity of our preparations; it was possible that the very few atoms present were simply carried along, neither increasing nor decreasing.

In order to test this, we then carried out identical experiments with equally small activity, using the natural radium isotopes, mesothorium and thorium X. These substances were obtained in a state of pure radioactivity, that is, separated from the parent substances and transformation products, and subjecteel to the same crystallization methods as we had used with our artificial preparations. The result was the one to be expected for radium. Both mesothorium and thorium X became concentrated in the right fractions to a degree which coincided with our earlier results many years before. Here was the proof that even a very few atoms of natural radium isotopes reacted in exactly the same way as strong concentrations.

Finally we changed over to the direct " indicator experiments," first introduced into radiochemistry by Hevesy and Paneth. We mixed the pure *natural* radium isotopes with our *artificial* " radium isotopes "—previously purified from their transformation products—and proceeded with our fractional crystallization as before. *In the end products the natural radium isotopes were separated from barium, the artificial ones were not.*

Furthermore we undertook exactly analogous experiments with the direct disintegration products of our artificial radium isotopes and with the actinium isotope, mesothorium 2, obtained from mesothorium. The actinium isotopes was separable from lanthanum (which had been added as carrying agent), but the artificial transformation products were not—they were chemically identical with lanthanum. In this way we had once again ascertained that our alkaline-earth isotopes which we had till then taken to be radium isotopes were in reality artificial barium isotopes whose β-radiation produced lanthanum, but not actinium.

I need not detail the rest of these experiments. At the time of our first publication, the measurements of the indicator experiments of which I have spoken were not yet quite complete

and we therefore expressed ourselves still cautiously. But by then it was already impossible that we could be mistaken.

That first publication appeared at the beginning of January 1939; in a second publication at the beginning of February, we stated that thorium too is split by fast neutrons and we were able to demonstrate the second partner in the fission process to be the active rare gas, krypton. The sum of the atomic numbers 56 for barium and 36 for krypton makes up 92—uranium.

Immediately after our first publication on the chemical proof of barium isotopes obtained from uranium, Lise Meitner and Otto Robert Frisch explained this process, using Bohr's model of the atom, and made an estimate of the immense amount of energy released through the splitting, as shown by the mass-defect curve of the elements of the Periodic System. It was Meitner and Frisch who coined the word "fission."

A glance at the atomic weights of the relevant fission products, compared with the atomic weight of uranium, immediately showed us that the new artificial atoms must have much too high atomic weights, that they were therefore unstable and would be transformed by β-radiation into atoms of higher elements. Indeed it was through their activities that Strassmann and I had discovered the fission. We also spoke of the possibility that superfluous neutrons were evaporated in order to compensate for the too high atomic weights.

The proof of the emission of such additional neutrons during the fission process was discovered by Joliot, von Halban, and Kowarsky, as well as by American research workers. With this evidence that two or three (more accurately 2·56) additional neutrons are generated with the fission of uranium, chain reactions had become a possibility.

But even as early as 1939 it was recognized that the processes were much more complex than had originally been assumed. The fission only takes place in the case of the rare uranium isotope 235, while the much commoner uranium 238 is not split by the slow neutrons that we used. By emitting β-rays it is transformed into the next higher element, that is into a genuine transuranic element with the nuclear charge 93. This element, in its turn, again emitting β-rays, is transformed into the next higher element 94.

Dr. Meitner and I had found the beginning of these processes several years before in a β-ray-emitting artificial uranium isotope with a half-life period of 23 minutes; but with our weak radiation sources we had been unable to find the transformation products. Later these elements were discovered in the United States; element 93 was called neptunium and its successive product, element 94, became known as plutonium.

The atoms which were taken to be transuranic before the discovery of nuclear fission—first by Fermi and then by us—were all fission products, that is medium heavy elements.

In the year 1939 there was a very lively international and completely unrestricted discussion on the chemical and physical consequences of the newly discovered nuclear process. But in the autumn of 1939, with the outbreak of the second world war, silence reigned in the nuclear-physics institutes of the world.

The rest is a matter of general knowledge. The bombs on Hiroshima and Nagasaki showed what had been done in barely five years by the combined work of American, English, and Canadian physicists and chemists, helped by refugee scientists from Germany, Italy, and France. In Germany atomic physicists had also found that an energy-producing chain reaction was possible; it was however absolutely impossible to try to produce atom bombs during the war, and many scientists were glad not to have to shoulder such a gigantic responsibility.

We chemists in the Kaiser-Wilhelm Institute for Chemistry did not participate in the work of the physicists. We were interested in the clarification of the very complex fission processes and the isolation of the numerous isotopes. By the spring of 1945 we had set up a table of 25 different elements with more than 100 direct or indirect fission products of uranium. Even during the war we published all our results. The first comprehensive large-scale Table in the United States did not appear till after the war, nearly two years later. Strassmann and I felt a certain satisfaction when we found that the American Table included a number of half-lives merely designated as "short," which we, with our primitive means, had been able to pinpoint more precisely. The American radiation sources were of such intense strength that no such rapid work was possible.

We developed this isolation of short-lived transformation products almost as a sport. Thus, apart from a series of more stable alkali metals, we were able to isolate completely—that is, separate from the numerous other fission products—an active cæsium isotope with a half-life of about 40 seconds and an active strontium isotope with one of 80 seconds. In order to do

this, we had recourse to the method I had introduced many years before, using radioactive rare gases, the so-called emanation method.

To obtain the short-lived alkali metals which arise in the fission from the still shorter-lived krypton and xenon isotopes, we used uranium preparations with a high emanation capacity, from which a large percentage of the active rare gases diffused at normal temperature despite their very short half-lives. On a negatively charged plate we collected the alkali metals as "active deposits." It was then possible to go to work so quickly on the invisible mixture of substances precipitated on to the plate that we were able, for instance, to register cæsium on our counter as cæsium silicotungstate 1·2—1·4 minutes after interrupting the radiation. By other methods, the time taken for the mixture cæsium–rubidium (separated from all other products) was 1·6—1·8 minutes.

When examining the very complicated mixtures of the rather longer-lived transformation products of the rare gases, we operated in the following way: During the irradiation of the uranium solution, the rare gases were passed through various freezing mixtures, one of which condensed the radioactive xenon while another condensed the krypton. In this way we had a direct method of separating the isotope group cæsium–barium–lanthanum from the group rubidium–strontium–yttrium.

I have come to the end of my survey. In August last year Dr. Strassmann and I attended the International Conference on the Peaceful Uses of Atomic Energy. We were extremely impressed by what we heard and what was shown to us there. In particular, we saw the quite extraordinary development attained in atomic nuclear research, not only in U.S.A., but also in England as well under the guidance of Sir John Cockcroft.

Wonderful indeed are the perspectives being opened up for the use of atomic energy in peace—may they blot out entirely the suicidal prospects of the use of atom and hydrogen bombs in war!

## PRESIDENTIAL ADDRESS.

DELIVERED AT THE 115TH ANNIVERSARY MEETING OF THE CHEMICAL SOCIETY AT THE UNIVERSITY OF NOTTINGHAM ON MARCH 27TH, 1956.

# *Alkoxides Old and New.*

By W. WARDLAW, C.B.E., D.Sc., F.R.I.C.

FELLOWS of the Chemical Society when meeting in Nottingham cannot fail to recall with pride the fruitful and distinguished work which was done in this University on organic compounds of silicon by a former Fellow of the Society—Professor F. S. Kipping. Perhaps it is fitting that at this Anniversary Meeting, the President of the Chemical Society should address you on a related topic.

Although we are warned against the deceitfulness which lurks in generalities, like other warnings it has more often proved an incentive rather than a deterrent. So, undismayed by the attendant risks, I propose to re-examine today a generalisation I outlined last year in my Presidential Address.

The results presented in Table I seem to establish the claim that the structure and volatility of the alkoxides of some Group IV elements are governed by the configuration of the alkyl groups and the atomic radius of the central metal atom. The boiling points (at 0·1 mm.) and molecular complexity (in parentheses) are given of selected compounds having an increasing degree of chain branching of the alkyl group.

TABLE I.

| | Si | Ti | Zr | Th |
|---|---|---|---|---|
| Atomic radius (Å) | 1·17 | 1·36 | 1·48 | 1·65 |
| Alkoxyl | | | | |
| O·$CH_2Me$ | −15° * (1·0) | 102° (2·4) | 180° (3·4) | Non-volatile |
| O·$CHMe_2$ | 15 (1·0) | 49 (1·4) | 160 (3·0) | 210° (3·8) |
| O·$CMe_3$ | — | 52 (1·0) | 50 (1·0) | 160 (3·4) |
| O·$CMeEt_2$ | — | 128 (1·0) | 128 (1·0) | 148 (1·8) |
| O·$CEt_3$ | — | 166 (1·0) | 166 (1·0) | 154 (1·0) |

* Calculated.

An interesting feature of Table I is the behaviour of the monomeric tertiary $C_7$ alkoxides of titanium, zirconium, and thorium. Their boiling points are close together, suggesting that they have similar molar heats of vaporisation because the effect of the central atom has been obviated by the screen of organic groups. This emphasises the powerful effect of highly branched alkoxide groups in shielding a central atom. Thus, in addition to suppressing the intermolecular attraction involving the central atom and oxygen, it appears that the contribution due to the marked ionic character in the thorium alkoxide is also nullified. The widely accepted view that volatility decreases with rising molecular weight is not supported by the data in Table I. In fact the volatility of the monomeric thorium alkoxide $Th(O{\cdot}CEt_3)_4$ is greater than that of the corresponding monomeric alkoxides of zirconium and titanium. An important feature of the alkoxides of zirconium and hafnium is that for analogous compounds the order of volatility is Hf > Zr although the atomic weights of the elements are 178·6 and 91 respectively. Actually the fundamental effect of mass on volatility has a theoretical background and explains certain boiling-point anomalies. In the case last mentioned it follows from the Clausius–Clapeyron equation that the relative volatility $P_{Zr}/P_{Hf}$ over a small temperature range will take the form :

$$\log_{10} P_{Zr}/P_{Hf} = (a_{Zr} - a_{Hf}) - (b_{Zr} - b_{Hf})/T$$

In the case where $b_{Zr} \simeq b_{Hf}$ the temperature-independent terms $a_{Zr}$ and $a_{Hf}$ will assume major importance. It is noteworthy that for the relative volatilities $P_1/P_2$ of solid monatomic compounds the difference between the temperature-independent terms $a_1$ and $a_2$ can be calculated by the method of statistical thermodynamics and reduces to the simple form $a_1 - a_2 = \frac{3}{2} \log_{10} M_1/M_2$, where $M_1$ and $M_2$ are the molecular weights. Hence for $b_1 = b_2$ it follows that $\log_{10} P_1/P_2 = \frac{3}{2} \log_{10} M_1/M_2$ and the substance with the greater molecular weight is the more volatile. For polyatomic molecules $a_1 - a_2$ will exceed $\frac{3}{2} \log_{10} M_1/M_2$ by an amount

which is determined by a function of the ratios of the various moments of inertia, *e.g.*, $\frac{1}{2}\log_{10}(I_A \times I_B \ldots I_H/I_P \times I_Q \ldots I_Z)$, and whose complexity depends on the number and arrangements of atoms in the molecule. Since molecular weight is included in the moment of inertia, it is evident that in polyatomic molecules (with $b_1 = b_2$) there is a possibility that this " molecular-weight effect " will enhance the greater volatility of the compound with higher molecular weight.

With regard to the *tert.*-amyloxides of zirconium and hafnium, the data show $b_{Hf} > b_{Zr}$ and $a_{Hf} > a_{Zr}$, which suggests that in spite of greater intermolecular attraction in the hafnium compound its higher molecular weight leads to a greater volatility. However, it is realised that a variation of 1% would reverse the orders to $a_{Zr} > a_{Hf}$ and $b_{Zr} > b_{Hf}$, and more accurate vapour-pressure determinations (now in progress) are required before a confident explanation for the observed volatility order can be advanced. It is noteworthy that in the borohydrides $M(BH_4)_4$,[1] which are the most volatile known compounds of zirconium or hafnium, the hafnium compound is the more volatile and again $a_{Hf} > a_{Zr}$ and $b_{Hf} > b_{Zr}$. Moreover, the relative volatility $P_{Hf}/P_{Zr}$ is greater in the borohydrides where $M_{Hf}/M_{Zr} = 1{\cdot}58$ than in the *tert.*-amyloxides where $M_{Hf}/M_{Zr} = 1{\cdot}18$, in qualitative agreement with the above theory.

A notable omission from the list of elements so far considered is cerium. The position of cerium in Group IVA of the Periodic Table is peculiar. It cannot be treated as a member of the linear series Ti–Zr–Ce–Hf–Th. More appropriately it may be regarded as one of the alternative links between zirconium and thorium, Ti–Zr$\begin{smallmatrix}\text{Ce}\\ \text{Hf}\end{smallmatrix}$Th. The atomic radii of hafnium and zirconium are identical and in the literature those of cerium and thorium are generally quoted as identical, 1·65 Å. To test how far the alkoxides of cerium fitted into the general pattern for alkoxides of Group IVA elements, my colleague, Dr. A. K. Chatterjee, began a study of these substances. At the time he started his investigation cerium alkoxides were unknown and it seemed possible that they would be difficult to isolate.

Of the available methods for the preparation of alkoxides those involving the use of the chloride had to be eliminated owing to the non-existence of a tetrachloride of cerium. Any attempts to prepare the alkoxides of quadrivalent cerium were thus limited to the methods involving the pyridinium cerium hexachloride and thus suggested the following possibilities :

$$(1)\quad (C_5H_6N)_2CeCl_6 + 6NH_3 + 4ROH = Ce(OR)_4 + 6NH_4Cl + 2C_5H_5N$$

$$(2)\quad (C_5H_6N)_2CeCl_6 + 6NaOR = Ce(OR)_4 + 6NaCl + 2ROH + 2C_5H_5N$$

Preliminary experiments showed that the most suitable starting material was the *iso*propoxide prepared by method (1). It was isolated first as $Ce(OPr^i)_4,C_5H_5N$. On recrystallisation from *iso*propyl alcohol a beautiful yellow crystalline alcoholate $Ce(OPr^i)_4,Pr^iOH$ was obtained. In this respect cerium behaves more like zirconium than thorium. Accordingly, for all subsequent work cerium *iso*propoxide was exclusively prepared by this method and converted into any other cerium alkoxide by alcohol interchange. The primary alkoxides prepared are listed in Table 2, together with the molecular weights determined ebullioscopically in benzene and in toluene. These substances are in general very readily hydrolysed and unstable even in dry air. The slight decrease in molecular complexity of the compounds in boiling toluene is due purely to the thermal effect of difference in boiling points of the solvents.

TABLE 2. *Primary alkoxides of cerium.*

| | | Benzene | | Toluene | |
|---|---|---|---|---|---|
| Alkoxide | Volatility | Mol. weight | Mol. complexity | Mol. weight | Mol. complexity |
| Methoxide $Ce(OMe)_4$ | Non-vol. | Insol. | — | — | — |
| Ethoxide $Ce(OEt)_4$ | Non-vol. | Insol. | — | — | — |
| *n*-Propoxide $Ce(OPr^n)_4$ | Non-vol. | 1618 | 4·3 | 1295 | 3·44 |
| *n*-Butoxide $Ce(OBu^n)_4$ | Non-vol. | 1819 | 4·21 | 1504 | 3·48 |
| *iso*Butoxide $Ce(OBu^i)_4$ | Non-vol. | 1814 | 4·20 | 1469 | 3·40 |
| Pentyloxide $Ce(O{\cdot}CH_2Bu^n)$ | Non-vol. | 2050 | 4·2 | 1665 | 3·41 |
| *neo*Pentyloxide $Ce(O{\cdot}CH_2Bu^t)_4$ | B. p. 260°/0·01 mm. | 1236 | 2·53 | 1202 | 2·46 |

Table 2 shows the following outstanding features : (*a*) the high molecular complexity of these compounds, except the *neo*pentyloxide; (*b*) the lack of appreciable effect of chain length on molecular complexity; (*c*) the anomalous behaviour of the *neo*pentyl oxide.

[1] Hoekstra and Katz, *J. Amer. Chem. Soc.*, 1949, **71**, 2488.

The only volatile cerium compound in this series is the *neo*pentyloxide, which sublimes unchanged at 260°/0·01 mm. and shows a surprisingly low molecular complexity of 2·5 in boiling benzene. As the *neo*pentyl group has a much greater steric hindrance than other primary alkyl groups, such anomalous behaviour of the *neo*pentyl grouping was not very surprising. The molecular complexities of the normal alkoxides of titanium, zirconium, and cerium in benzene are given in Table 3, and it is clear that molecular complexity is greater in cerium alkoxides than in the corresponding titanium and zirconium alkoxides. This can be explained as due to stereochemical effects or to a difference in strength of the intermolecular bonding or to a combination of both the factors. Thus cerium with an atomic radius of 1·65 Å will require more effective shielding than the smaller silicon, titanium or zirconium atom (Si = 1·17 Å; Ti = 1·36 Å; Zr = 1·48 Å).

TABLE 3. *Molecular complexities of normal alkoxides of* Ti, Zr, *and* Ce *in benzene.*

| Alkoxides | Ti | Zr | Ce |
|---|---|---|---|
| Ethoxide | 2·4 | 3·6 | — |
| Propoxide | — | — | 4·3 |
| Butoxide | — | 3·4 | 4·2 |
| Pentyloxide | 1·4 | 3·2 | 4·2 |

It is not surprising that the primary alkoxides of cerium are non-volatile and complex in nature, since the atomic radius of cerium equals that of thorium where the methoxide and ethoxide are insoluble non-volatile compounds.

In the secondary series the following compounds were prepared: $Ce(O{\cdot}CHR_2)_4$ where R = Me or Et, and $Ce(O{\cdot}CHMeR)_4$ where R = Et, Pr$^n$, or Pr$^i$. The *iso*propoxide was the only member of the series which responded to any attempt at sublimation. Table 4 summarises the

TABLE 4. *Secondary alkoxides of cerium.*

| | | Benzene | | Toluene | |
|---|---|---|---|---|---|
| Alkoxides | Volatility | Mol. wt. | Mol. complexity | Mol. wt. | Mol. complexity |
| *iso*Propoxide * $(O{\cdot}CHMe_2)_4Ce$ | B. p. 160—170°/0·05 mm. | 1179 | 3·13 | 1045 | 2·78 |
| *sec.*-Butoxide $(O{\cdot}CHMeEt)_4Ce$ | Non-volatile | 1293 | 2·99 | 1210 | 2·80 |
| 1-Methyl-*n*-butoxide $(O{\cdot}CHMePr^n)_4Ce$ | Non-volatile | 1520 | 3·11 | 1363 | 2·79 |
| 2 : 3-Dimethyl-*n*-propoxide $(O{\cdot}CHMePr^i)_4Ce$ | Non-volatile | 1464 | 3·00 | 1377 | 2·82 |
| 1-Ethyl-*n*-propoxide $(O{\cdot}CHEt_2)_4Ce$ | Non-volatile | 1420 | 2·90 | 1370 | 2·80 |

* Mol. wt. of *iso*propoxide in propan-2-ol = 850 and hence mol. complexity = 1·99.

results. The most striking point brought out by this Table is the non-volatile and complex nature of the secondary alkoxides. All the corresponding titanium *sec.*-alkoxides (with the exception of the lowest member) are monomeric, whereas in zirconium the complexity of the secondary alkoxides changes from 3 to 2 to 1 as the alkyl groups in $Zr(O{\cdot}CHR_2)_4$ are changed from methyl to ethyl to propyl In the case of cerium all the compounds exhibit a complexity of 3 in boiling benzene whilst in toluene the complexity has declined to 2·8. This behaviour accords with the prediction that a rise in temperature of the solvent should cause dissociation of the trimers. A glance at Table 5 shows how the size of the central atom plays a decisive

TABLE 5. *Volatilities and molecular complexities of* iso*propoxides of* Si, Ti, Zr, Ce, *and* Th.

| Elements | Atomic radii (Å) | *iso*Propoxide | Volatility (B. p.) | Molecular complexity | |
|---|---|---|---|---|---|
| | | | | Benzene | Propan-2-ol |
| Si | 1·17 | $Si(OPr^i)_4$ | 15°/0·1 mm. | 1·0 | — |
| Ti | 1·36 | $Ti(OPr^i)_4$ | 49°/0·1 mm. | 1·4 | — |
| Zr | 1·48 | $Zr(OPr^i)_4$, $Pr^iOH$ | 160°/0·1 mm. | 3·0 | 2 |
| Ce | 1·65 | $Ce(OPr^i)_4$, $Pr^iOH$ | 170°/0·05 mm. | 3·1 | 1·99 |
| Th | 1·65 | $Th(OPr^i)_4$ | 210°/0·05 mm. | 3·8 | 1·84 |

part in the structure of the *iso*propoxides. The larger the atom the greater would be its shielding requirements. Four *iso*propoxy-groups are sufficient to shield the small silicon atom, whereas already in titanium the shielding is incomplete till finally, on coming to the bigger atoms of zirconium, cerium, and thorium, incomplete shielding gives rise to higher complexity.

The tertiary alkoxides of quadrivalent cerium proved to be especially interesting from the stereochemical viewpoint. The following new alkoxides were prepared :

$Ce(OR)_4$ where R = $CMe_3$, $CMe_2Et$, $CMeEt_2$, $CEt_3$, $CMe_2Pr^n$, $CMe_2Pr^i$, and $CMeEtPr^n$.

All were prepared by alcohol interchange involving the crystalline cerium *iso*propoxide and the appropriate alcohol. These represent the only volatile compounds of quadrivalent cerium yet recorded. The tertiary butoxide and the tertiary amyloxides were yellow crystalline solids whilst the other tertiary alkoxides were yellow liquids which could be distilled unchanged. The data, including volatility and molecular complexity, are summarised in Table 6.

TABLE 6. *Tertiary alkoxides of cerium.*

| | | Benzene | | Toluene | |
|---|---|---|---|---|---|
| Alkoxides | Volatility (B. p.) | Mol. wt. | Mol. compl. | Mol. wt. | Mol. compl. |
| *tert.*-Butoxide $(O{\cdot}CMe_3)_4Ce$ ..... | 140—150°/ 0·01 mm. | 1062 | 2·46 | 968 | 2·24 |
| *tert.*-Amyloxide $(O{\cdot}CEtMe_2)_4Ce$ ..... | 240°/0·01 mm. | 1150 | 2·36 | 1050 | 2·15 |
| 1 : 1-Dimethyl-*n*-butoxide $(O{\cdot}CPr^nMe_2)_4Ce$ ..... | 140°/0·06 mm. | 746·2 | 1·37 | 580·4 | 1·06 |
| 1 : 1 : 2-Trimethyl-*n*-propoxide $(O{\cdot}CPr^iMe_2)_4Ce$ | 146°/0·05 mm. | 761·7 | 1·40 | 600 | 1·1 |
| 1-Ethyl-1-methyl-*n*-propoxide $(O{\cdot}CEt_2Me)_4Ce$ ... | 132°/0·05 mm. | 584 | 1·07 | 541·6 | 0·99 |
| 1 : 1-Diethyl-*n*-propoxide $(O{\cdot}CEt_3)_4Ce$ ..... | 154°/0·05 mm. | 650·3 | 1·08 | 604·7 | 1·00 |
| 1-Ethyl-1-methyl-*n*-butoxide $(O{\cdot}CMeEtPr^n)_4Ce$... | 150°/0·05 mm. | 604·5 | 1·00 | — | — |

The data reveal that all *tert.*-alkoxides of cerium are volatile, that volatility and molecular complexity vary with shape and size of the alkyl groups, and that for a given alkoxide molecular complexity is always lower in toluene than in benzene (except when the alkoxide is monomeric in benzene). All these findings are consistent with the stereochemical theory already advanced to account for the behaviour of the alkoxides of silicon, titanium, zirconium, hafnium, and thorium. This theory explains the associated and non-volatile nature of primary and secondary alkoxides as due to the intermolecular bonding M· · ·O involving a central metal atom and oxygen from a neighbouring alkoxide group. The steric hindrance of tertiary alkyl groups prevents such co-ordination and tertiary alkoxides are therefore less complex. In the monomeric alkoxides the central atom is sufficiently shielded by the rotation of the branched alkoxide groups to prevent any co-ordination and a volatile compound results.

A comparison of the properties of the tertiary alkoxides of Group IVA elements with regard to their shielding requirements is very interesting. For example, tetra-*tert.*-butoxysilane has only recently been prepared owing to the difficulty of replacing four halogen atoms by tertiary butoxide groups around the small silicon atom. In the cases of titanium and zirconium the shielding by the *tert.*-butoxide groups is sufficient to produce monomeric compounds which are the most volatile alkoxides of these elements. Finally, the thorium atom is so large that screening by four *tert.*-butoxides does not prevent polymerisation so that thorium *tert.*-butoxide is complex and much less volatile than the titanium and zirconium compounds. In fact the higher tertiary alcohol (triethylcarbinol) is required to produce a monomeric thorium alkoxide. The behaviour of cerium resembles that of thorium in this respect although the lower complexity of the cerium derivative of 3-methylpentan-3-ol (diethylmethylcarbinol) suggests that cerium may have a smaller atomic radius than thorium. The order of shielding efficiency of different tertiary $C_6$ alkyloxide groups as judged by the molecular complexity of their thorium derivatives was found to be $(O{\cdot}CMeEt_2) > (O{\cdot}CMe_2Pr^i) > (O{\cdot}CMe_2Pr^n)$. The same order obtains in the case of the cerium derivatives.

TABLE 7. *Boiling points (in* °C/0·1 *mm.* Hg) *and molecular complexities (in parentheses) of* $M(O{\cdot}CMe_nEt_{3-n})_4$.

| *n* | Ti | Zr | Ce | Th |
|---|---|---|---|---|
| 3 | 52° (1) | 50° (1) | 150° (2·4) | 160° (3·4) |
| 2 | 98 (1) | 95 (1) | 240 (2·3) | 198 (2·8) |
| 1 | 128 (1) | 128 (1) | 132 (1) | 148 (1·8) |
| 0 | 166 (1) | 166 (1) | 154 (1) | 154 (1) |

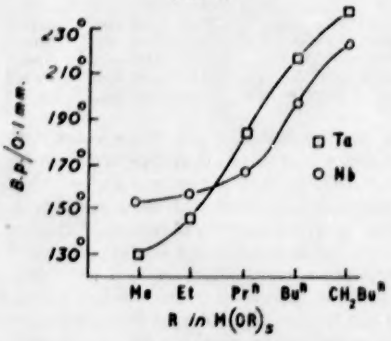
A comparison of the tertiary alkoxides $Ce(O{\cdot}CMe_nEt_{3-n})_4$ with the analogous compounds of other elements of Group IVA is shown in Table 7. The data in this Table give a definite indication that the atomic radius of cerium may not be identical with that of thorium and is really a little smaller.

Another interesting feature is the behaviour of the monomeric tertiary $C_7$ alkyloxides of titanium, zirconium, cerium, and thorium. The relative volatility of the analogous monomeric *n*-heptyloxides is Ce = Th > Zr = Ti, whereas the molecular weights of these compounds are in the order Ti < Zr < Ce < Th. This order of volatility is, however, in conformity with the theory of the fundamental effect of mass on volatility. Nevertheless, it must be pointed out that the effect of molecular mass on volatility is very small compared with the part played by the latent heat of vaporisation, and it is still an open question whether the order of volatilities of these compounds is a result of differences in latent heats or molecular mass.

To ascertain how widely the stereochemical theory could be applied we thought it would be worth while to examine the properties of the alkoxides of some Group V elements. For this purpose we selected niobium and tantalum as they have identical atomic radii but very different atomic weights (93·3, 181·4). In their alkoxides the fundamental effect of mass on volatility might well be apparent.

Perusal of the literature showed that little attention had been given to the study of organic

FIG. 1.




compounds of these elements. The reaction between ethyl alcohol and niobium or tantalum pentachloride was known to take place according to the equation :

$$MCl_5 + 3EtOH = MCl_2(OEt)_3 + 3HCl$$

However no mention was made in the literature of niobium or tantalum penta-alkoxides. Recently Miss A. Whitley and B. N. Chakravarti have shown that a range of such alkoxides can be made by the general reaction :

$$MCl_5 + 5ROH + 5NH_3 = M(OR)_5 + 5NH_4Cl$$

(where M = Nb, Ta; R = Me, Et, $Pr^n$, or $Bu^n$).

The method of alcohol interchange was particularly useful in the preparation of pure normal alkoxides. However, we found that a fully substituted secondary or tertiary alkoxide of niobium or tantalum cannot be prepared by the alcohol-interchange process. Only four out of the five primary alcohol groups can be replaced by a secondary alcohol acting upon niobium and tantalum alkoxides. Four tertiary groups can be introduced by alcohol interchange into tantalum penta-primary or penta-secondary alkoxides. Such compounds of tantalum, $Ta(OR)(OR')_4$ where R = a primary or secondary group and R′ = a tertiary group, are quite stable and volatile. When a primary alkoxide of niobium reacted with a tertiary alcohol, practically the whole of the primary alcohol group was replaced and the product had the composition $Nb_2O(OR^t)_8$. These experiments established the fact that the failure to obtain penta-tertiary alkoxides of niobium is due to some specific property of niobium itself.

Additional interest was centred on the relative volatilities of corresponding niobium and tantalum alkoxides because of the possibility that the fundamental effect of molecular weight on volatility might be apparent. The boiling points of niobium and tantalum alkoxides under reduced pressure are given in Table 8. The striking feature of these data is the dependence of the relative volatility of niobium and tantalum normal alkoxides on the length of the alkyl chain. Thus it is clear that for the methoxides and alkoxides the tantalum compound is the

more volatile, whilst for the higher normal alkoxides the niobium compound is the more volatile. Moreover this occurs in both the pressure ranges investigated. These results suggest that the separation of niobium and tantalum by distillation of the alkoxides should be relatively simple, and this is now being investigated. The molecular weights of the niobium and tantalum *n*-alkoxides were determined ebullioscopically in benzene, in toluene, and in the parent alcohols and the molecular complexities are given in Table 9.

TABLE 8.

| R in $M(OR)_5$ | M. p. | | Boiling point (°c/mm. Hg) Lower pressure | | Higher pressure | | Molecular complexity | |
|---|---|---|---|---|---|---|---|---|
| | Nb | Ta | Nb | Ta | Nb | Ta | Nb | Ta |
| Me ..... | 60° | 50° | 153°/0·12 | 130°/0·2 | 200°/5·5 | 189°/10 | 2·11 | 1·98 |
| Et ..... | Liq. | Liq. | 156·5°/0·05 | 146·5°/0·15 | 207·5°/5·5 | 202°/10 | 2·02 | 1·98 |
| $Pr^n$ ..... | ,, | ,, | 166°/0·04 | 184°/0·15 | 218·5°/5·5 | 232°/10 | 2·02 | 1·95 |
| $Bu^n$ ..... | ,, | ,, | 197°/0·15 | 217°/0·15 | 230°/5·5 | 256°/10 | 2·01 | 2·02 |
| $Am^n$ ..... | ,, | ,, | 223°/0·15 | 239°/0·2 | — | — | 2·00 | 2·01 |

TABLE 9.

| R in $M(OR)_5$ | Molecular complexity: Benzene [a] | | Toluene [b] | | Parent alcohol | |
|---|---|---|---|---|---|---|
| | Nb | Ta | Nb | Ta | Nb | Ta |
| Me ..... | 2·11 | 1·98 | 1·90 | 1·83 | 1·34 [c] | 1·20 |
| Et ..... | 2·02 | 1·98 | 1·89 | 1·83 | 1·52 [d] | 1·78 |
| $Pr^n$ ..... | 2·02 | 1·95 | 1·79 | 1·83 | 1·29 [e] | 1·70 |
| $Bu^n$ ..... | 2·01 | 2·02 | 1·74 | 1·83 | 1·13 [f] | 1·40 |
| $Am^n$ ..... | 2·00 | 2·01 | — | — | — | — |

[a] Benzene: b. p. 80·3°, D.C. 2·28. [b] Toluene: b. p. 110°, D.C. 2·38. [c] Methyl alcohol: b. p. 64°, D.C. 33·1. [d] Ethyl alcohol: b. p. 78°, D.C. 24. [e] *n*-Propyl alcohol: b. p. 97°, D.C. 22·2. [f] *n*-Butyl alcohol: b. p. 117°, D.C. 17·7.

All the niobium and tantalum *n*-alkoxides are dimeric in boiling benzene and it seems likely that these metals are 6 co-ordinate. Evidence for the dissociation of these dimers at a higher temperature is apparent from the results in boiling toluene. However, there is a significant difference between the behaviour of niobium and of tantalum alkoxides in this solvent. Whilst the *n*-alkoxides of tantalum all have the same complexity, there is a distinct decrease in complexity with increase in alkyl-chain length for the niobium compounds. We infer from these results that the energy of depolymerisation is sensibly constant for the tantalum series but decreases with increase in the alkyl chain for the niobium *n*-alkoxides. Further, this explanation is quantitatively consistent with the dependence of relative volatility of niobium and tantalum *n*-alkoxides on the chain length of the alkyl group. Thus the energy of depolymerisation will be included in molar heat of vaporisation,

$$L_v = L_{mon.} + E$$

where $L_v$ = molar heat of vaporisation, $L_{mon.}$ = hypothetical heat of vaporisation of "monomeric" alkoxide, and $E$ = energy of depolymerisation. It seems reasonable to assume that $L_{mon.}$ for a niobium alkoxide will be close to that for a corresponding tantalum compound, and differences in $E$ will therefore be reflected as differences in $L_v$.

If now $E\{Nb(OMe)_5\} > E\{Ta(OMe)_5\}$, then according to the view that $E$ for tantalum *n*-alkoxides is constant whilst $E$ for niobium *n*-alkoxides varies in the order: methoxide > > ethoxide > *n*-propoxide > *n*-butoxide > *n*-pentyloxide, it seems quite possible that the values of $L_v$ will be $Nb(OMe)_5 > Ta(OMe)_5$, $Nb(OEt)_5 > Ta(OEt)_5$, and $Nb(OR)_5 < Ta(OR)_5$ where R = $Pr^n$, $Bu^n$, or *n*-$C_5H_{11}$. This postulated order of $L_v$'s is in agreement with the order of boiling points given in Table 8. Some support for this argument is forthcoming from the complexities of the alkoxides in their parent alcohols. It has been suggested that the primary factors causing dissociation of tantalum *n*-alkoxides in their boiling parent alcohols are (1) boiling point of solvent (temperature effect) and (2) "donor" power of solvent (solvation effect). The same arguments must apply to niobium alkoxides, and hence it is deduced that $E\{Nb(OMe)_5\} > E\{Ta(OMe)_5\}$, and $E\{Nb(OR)_5\} < E\{Ta(OR)_5\}$, where R = Et, $Pr^n$, $Bu^n$. Only in the case of the ethoxide does the order of $E$'s conflict with that suggested above for

$L_v$'s. It is clear that vapour-pressure data will give valuable information concerning these phenomena.

Since the atomic radii of niobium and tantalum are the same (1·34 Å) these differences in the behaviour of their alkoxides must be ascribed to electronic factors. It is well known that niobium differs from tantalum in having a pronounced tendency to form any compounds containing the niobium–oxygen double bond, and hence there will be a greater tendency for covalency expansion involving " intramolecular " bonding as in $(RO)_4\bar{N}b{=}\overset{+}{O}R$ to compete with the intermolecular bonding which causes dimerisation. This will clearly lead to a readier depolymerisation with increase in temperature for the niobium compounds than for the tantalum derivatives. This ready double bonding between niobium and oxygen may also explain the lower thermal stability of the niobium alkoxides which will tend to split off carbonium ions : $Nb(OR)_5 = [(RO)_4\bar{N}b{=}O] + \overset{+}{R}$. This mechanism will be enhanced by the $(+I)$ electron-releasing tendency of the alkyl group and is in accord with the observed decrease in stability of niobium *n*-alkoxides with increase in chain length of the alkyl group.

According to current views on the effect of molecular weight on volatility, there should be a tendency for the heavier tantalum alkoxides to be more volatile than the corresponding niobium compounds although this effect is usually obscured by the differences in molar heats of vaporisation. However, we have already pointed out that the molecular complexities of the ethoxides in ethyl alcohol imply that $E\{Ta(OEt)_5\} > E\{Nb(OEt)_5\}$ and hence $L_v\{Ta(OEt)_5\} > L_v\{Nb(OEt)_5\}$ which would predict the order of volatilities $Nb(OEt)_5 > Ta(OEt)_5$. The observed order of volatilities $Ta(OEt)_5 > Nb(OEt)_5$ might well be due to the " mass effect " over-ruling the unfavourable order of latent heats. This problem should be resolved when vapour-pressure data are available.

It was evident that a study of the physicochemical properties of the alkoxides would be worth while, and with this in view measurements of the density, surface tension, vapour pressure, and viscosity of a range of alkoxides have been made. The parachor has been of great value in connection with the interpretation of structural abnormalities in compounds, especially as a result of recent work. It now seems well established that the volume contribution of any atom must vary with the nature of the other atoms to which it is attached. Consequently, the old idea of atomic parachors is severely restricted in application and, instead, Gibling has evaluated a set of group parachors. Thus, in hydrocarbons the methyl group when attached to carbon $CH_3{-}(C)$ = **55·2** units whilst the methylene group attached to two carbons $(C){-}CH_2{-}(C)$ = **39·8** units but methylene attached to carbon and to oxygen $(C){-}CH_2{-}(O)$ = **39·4**. These are standard values used by us in evaluating the calculated $[P]$ of a substance. These values are corrected for various other structural factors which may obtain in a particular molecule. Thus there is the correction for interference between non-bonded atoms which leads to a reduction in the parachor. Further corrections involve the bending of chains of atoms and also alignment of parallel chains. It appears from the data on organic compounds that there is an expansion effect in which the observed parachor is slightly greater than the calculated parachor to an extent which increases steadily with the size of the molecule.

Gibling's method may be illustrated by calculating the standard parachor for the group comprising a titanium atom and four oxygen atoms, the latter being joined to carbon atoms, *i.e.*, $[P]\ Ti[O(C)]_4$. For this purpose the experimental $[P]$ for titanium *tert.*-butoxide is selected because this is a monomeric alkoxide. The experimental parachor $[P]$ = **842·8** and this must be corrected for the expansion effect. To arrive at the corrected standard value the experimental parachor is divided by $(1{\cdot}0004165)^n$ where $n$ = number of atoms other than hydrogen in the molecule. Thus the corrected standard value = **842·8**/1·0072 = **836·7**. A summation of the standard parachors for four tertiary butyl groups attached to oxygen atoms is given as follows :

$$\begin{aligned} 12 \times CH_3(C) &= 662{\cdot}4 \text{ units} \\ 4 \times \begin{matrix}(C)\\(C)\\(C)\end{matrix}\!\!\rangle C{-}(O) &= \quad 4{\cdot}8 \text{ units} \\ &\overline{\qquad\qquad} \\ &667{\cdot}2 \text{ units} \end{aligned}$$

After allowance for the correction (−**2·8**) for **4** carbon atoms attached to oxygen atoms, this gives a corrected standard value = **664·4** units. Hence the standard value for $Ti[O{-}(C)]_4$ = **836·7** − **664·4** = **172·3** units. This value has been used for the calculations in Table **10**. The parachor data show in a striking way that the titanium *n*-alkoxides are exhibiting some structural abnormalities. The very considerable contraction of *ca.* **95** units in each compound

is entirely consistent with the view that these molecules are trimeric in the liquid state. The phenomena of evaporation, surface formation, and flow of pure liquids all involve the breaking of bonds between molecules. According to current theories it should be possible by comparing

TABLE 10.

| Compound | [*P*], experimental | [*P*], calculated | Δ[*P*] |
|---|---|---|---|
| $Ti(OEt)_4$ | 453·7 | 550·6 | 96·9 |
| $Ti(OPr^n)_4$ | 615·8 | 708·5 | 92·7 |
| $Ti(OBu^n)_4$ | 768·2 | 863·6 | 95·4 |

the energy of vaporisation ($E_v$), the work of cohesion ($W_c$), and the energy of activation of viscosity ($E_{visc.}$) to obtain some insight into the structural aspects of the liquid alkoxides. Eyring has proposed an ingenious theory of the flow of liquids. He regards viscous flow as related to vaporisation, so that the energy required to create a hole of molecular dimensions inside a liquid is given by the energy of vaporisation defined as follows:

$$E_v = L_v - \boldsymbol{R}T$$

$L_v$, the molar heat of vaporisation, is calculated from the relationship $\log_{10} P = \text{constant} - L_v/2{\cdot}303\boldsymbol{R}T$. $\boldsymbol{R}T$ is the molar work of expansion involved in the passage from liquid to vapour. It seems reasonable to suppose that the condition for movement is that molecules should possess sufficient kinetic energy to push others out of their way. This is the basis of Eyring's theory of viscous flow. He suggests that, although it is necessary for a hole to be present into which the flowing molecule may pass, this hole may only be a fraction of the full size of a molecular hole and hence the free energy of activation for viscous flow ($\Delta F^\bullet$) should be some fraction of the energy of vaporisation $E_v$. For a wide range of compounds, including associated liquids but excluding metals, the ratio of $E_v$ to $\Delta F^\bullet$ was found to be sensibly constant, *i.e.*, $E_v/\Delta F^\bullet \cong 2{\cdot}45$. Thus it appears that the free energy of activation for viscous flow is approximately one-third of the energy of vaporisation. From the experimental determination of viscosity ($\eta_l$) at different temperatures the important quantities, $E_{visc.}$ and $\Delta F^\bullet$, may be deduced.

$$\log \eta_l = E_{visc.}/2{\cdot}303\boldsymbol{R}T - \text{constant}$$

$$\eta_l = \left(\frac{\boldsymbol{h}\boldsymbol{N}}{v}\right) e^{\Delta F^\bullet/\boldsymbol{R}T}$$

The ratio $E_v/E_{visc.}$ is usually between 3 and 4 except for metals and long-chain hydrocarbons. Hence the energy of activation of viscosity is approximately one-quarter of the energy of vaporisation.

Some data for the metal alkoxides obtained by Dr. C. C. A. Prevedorou are presented in Table 11 together with the ratios $E_v/\Delta F^\bullet$ and $E_v/E_{visc.}$. It is noticeable that for each alkoxide the ratios $E_v/\Delta F^\bullet$ and $E_v/E_{visc.}$ are practically temperature-independent. The ratio $E_v/\Delta F^\bullet$ is uniformly equal to 3 for all except the complex normal alkoxides and the "abnormal" derivatives of 2-methylpentan-2-ol (dimethyl-*n*-propylmethanol). This ratio is near to Eyring's value of 2·45, and the discrepancy is probably caused by the fact that his values of $E_v$ were calculated at the temperatures of normal boiling points whilst the values in Table 11 were calculated from the latent heats at temperatures well below the boiling points. Similarly, the values of $E_v/E_{visc.}$ are close to 3 and are usually very close to $E_v/\Delta F^\bullet$. It seems permissible to assume that the compounds in Table 11 with the ratios $E_v/\Delta F^\bullet$ and $E_v/E_{visc.} \sim 3$ are behaving normally with a mechanism of flow involving the movement of a sinple molecule over a potential gradient into an available hole. On the other hand, the titanium and zirconium derivatives of 2-methylpentan-2-ol (dimethyl-*n*-propylcarbinol) gives the abnormally high values of $E_v/\Delta F^\bullet \sim 3{\cdot}5$ and $E_v/E_{visc.} \sim 5$. This behaviour is consistent with the theory that in these compounds the unit of flow is smaller than a simple molecule. The data for the complex *n*-alkoxides of titanium are somewhat irregular. The values of $E_v/E_{visc.}$ less than 3 are consistent with the behaviour of complex molecules which have to dissociate either before evaporating or before engaging in viscous flow.

The viscosity data for the tertiary alkoxides are given in Table 12. All the tertiary alkoxides studied show values for the activation energy and free energy of viscosity which are independent of temperature over the range 25—40°.

TABLE 11.

| Compound | Temp. | $E_v$ (kcal./mol.) | $E_v/\Delta F^\circ$ | $E_v/E_{visc.}$ | $E_{visc.}/W_c$ | $E_v/W_c$ |
|---|---|---|---|---|---|---|
| $Ti(OEt)_4$ | 25° | 21·01 | 3·55 | 2·50 | 2·95 | 7·39 |
| | 30 | 21·00 | 3·55 | 2·50 | 2·96 | 7·39 |
| | 35 | 21·00 | 3·55 | 2·49 | 2·98 | 7·44 |
| | 40 | 20·98 | 3·55 | 2·49 | 2·98 | 7·44 |
| $Ti(OPr^n)_4$ | 25 | 15·11 | 2·18 | 1·71 | 2·33 | 3·99 |
| | 30 | 15·10 | 2·18 | 1·71 | 2·33 | 4·04 |
| | 35 | 15·10 | 2·18 | 1·70 | 2·40 | 4·10 |
| | 40 | 15·08 | 2·18 | 1·70 | 2·40 | 4·14 |
| $Ti(OBu^n)_4$ | 25 | 19·51 | 3·00 | 2·71 | 1·63 | 4·44 |
| | 30 | 19·50 | 3·00 | 2·71 | 1·64 | 4·50 |
| | 35 | 19·49 | 2·99 | 2·70 | 1·68 | 4·55 |
| | 40 | 19·48 | 2·99 | 2·70 | 1·68 | 4·56 |
| $Ti(OBu^s)_4$ | 25 | 14·00 | 2·91 | 3·41 | 0·83 | 3·00 |
| | 30 | 13·90 | 2·90 | 3·40 | 0·84 | 2·86 |
| | 35 | 13·89 | 2·90 | 3·39 | 0·85 | 2·90 |
| | 40 | 13·87 | 2·90 | 3·38 | 0·86 | 2·90 |
| $Zr(OBu^t)_4$ | 25 | 14·61 | 3·04 | 3·32 | 0·98 | 3·27 |
| | 30 | 14·59 | 3·03 | 3·31 | 1·00 | 3·32 |
| | 35 | 14·58 | 3·03 | 3·31 | 1·01 | 3·39 |
| | 40 | 14·57 | 3·03 | 3·31 | 1·04 | 3·44 |
| $Ti(O\cdot CMe_2Et)_4$ | 25 | 16·11 | 2·98 | 3·10 | 0·86 | 2·67 |
| | 30 | 16·09 | 2·97 | 3·09 | 0·87 | 2·67 |
| | 35 | 16·09 | 2·97 | 3·09 | 0·87 | 2·72 |
| | 40 | 16·09 | 2·97 | 3·09 | 0·88 | 2·73 |
| $Zr(O\cdot CMe_2Et)_4$ | 25 | 15·71 | 2·90 | 2·91 | 0·98 | 2·88 |
| | 30 | 15·69 | 2·90 | 2·91 | 0·99 | 2·88 |
| | 35 | 15·68 | 2·90 | 2·90 | 1·00 | 2·90 |
| | 40 | 15·67 | 2·90 | 2·90 | 1·01 | 2·95 |
| $Ti(O\cdot CPr^nMe_2)_4$ | 25 | 18·91 | 3·63 | 4·97 | 0·57 | 2·73 |
| | 30 | 18·90 | 3·63 | 4·97 | 0·57 | 2·75 |
| | 35 | 18·89 | 3·63 | 4·97 | 0·57 | 2·78 |
| | 40 | 18·80 | 3·63 | 4·97 | 0·58 | 2·83 |
| $Zr(O\cdot CPr^nMe_2)_4$ | 25 | 18·41 | 3·54 | 4·60 | 0·64 | 2·93 |
| | 30 | 18·40 | 3·54 | 4·60 | 0·64 | 2·97 |
| | 35 | 18·39 | 3·54 | 4·60 | 0·65 | 3·00 |
| | 40 | 18·38 | 3·54 | 4·60 | 0·65 | 3·03 |
| $Ti(O\cdot CEt_2Me)_4$ | 25 | 18·41 | 2·92 | 3·01 | 0·88 | 2·66 |
| | 30 | 18·40 | 2·92 | 3·01 | 0·89 | 2·68 |
| | 35 | 18·39 | 2·91 | 3·01 | 0·91 | 2·70 |
| | 40 | 18·39 | 2·91 | 3·01 | 0·91 | 2·75 |
| $Zr(O\cdot CEt_2Me)_4$ | 25 | 18·41 | 2·96 | 2·80 | 1·05 | 2·92 |
| | 30 | 18·40 | 2·96 | 2·79 | 1·05 | 2·93 |
| | 35 | 18·39 | 2·96 | 2·78 | 1·05 | 2·94 |
| | 40 | 18·39 | 2·96 | 2·78 | 1·06 | 2·96 |

TABLE 12.

| Alkoxide | $\eta$ | $\Delta F^\circ$ | $E_{visc.}$ | $\Delta S^\circ$ |
|---|---|---|---|---|
| $Ti(OBu^t)_4$ | 0·0352 | 4·8 | 4·1 | −2·4 |
| $Zr(OBu^t)_4$ | 0·0317 | 4·8 | 4·4 | −1·4 |
| $Ti(O\cdot CMe_2Et)_4$ | 0·0808 | 5·4 | 5·2 | −0·7 |
| $Zr(O\cdot CMe_2Et)_4$ | 0·0759 | 5·4 | 5·4 | 0 |
| $Sn(O\cdot CMe_2Et)_4$ | 0·1660 | 5·8 | 6·4 | +2·0 |
| $Ti(O\cdot CEt_2Me)_4$ | 0·3453 | 6·3 | 6·1 | −0·7 |
| $Zr(O\cdot CEt_2Me)_4$ | 0·2810 | 6·2 | 6·6 | 1·3 |
| $Ce(O\cdot CEt_2Me)_4$ | 1·0779 | 6·1 | 7·0 | 3·5 |
| $Sn(O\cdot CEt_2Me)_4$ | 0·4127 | 6·7 | 8·2 | 5·0 |
| $Ti(O\cdot CPr^nMe_2)_4$ | 0·0479 | 5·2 | 3·8 | −5·0 |
| $Zr(O\cdot CPr^nMe_2)_4$ | 0·0464 | 5·2 | 4·0 | −4·0 |
| $Ce(O\cdot CPr^nMe_2)_4$ | 8·1343 | 8·1 | 12·6 | 15·1 |
| $Sn(O\cdot CPr^nMe_2)_4$ | 0·0986 | 5·6 | 5·6 | 0 |
| $Ce(O\cdot CEt_3)_4$ | 0·5258 | 6·6 | 6·3 | −1·3 |
| $Th(O\cdot CEt_3)_4$ | 0·4920 | 6·6 | 7·6 | 3·5 |

It is instructive to compare the behaviour of titanium tetra-*tert.*-butoxide with that of its long-chain isomer, the *n*-butoxide :

| | Temp. | Viscosity | $\Delta F^\circ$ (kcal.) | $E_{visc.}$ | $\Delta S^\circ$ (cal.) |
|---|---|---|---|---|---|
| $Ti(OBu^n)_4$ | 25° | 0·6920 | 6·5 | 7·1 | 2·0 |

The remarkable effect of branching of the alkyl chain on physical properties is at once apparent. For example, the viscosity of the complex *n*-alkoxide is practically twenty times that of the *tert.*-alkoxide. This is reflected in the much greater free energy of activation of the *n*-butoxide, whilst its activation energy of viscosity approaches twice that of the *tert.*-isomer. By contrast, the difference in energies of cohesion is much smaller (*viz.*, *n*-butoxide $W_c = 4{\cdot}39$ kcal./mole; *tert.*-butoxide $W_c = 4{\cdot}92$ kcal./mole) and in the opposite sense. Clearly, the difference in $E_{visc.}$ is mainly the result of the depolymerisation energy requirements of the complex *n*-alkoxide and this is emphasised by the positive entropy of activation (2·0 cal./°/mole) for the *n*-isomer compared with the negative entropy of activation (−2·4 cal./°/mole) for the tertiary compound.

Some interesting features are immediately apparent if the data in Table 12 are considered from the viewpoint of the effect of changing the alkyl group in the case of a given metal atom. For example, the order of viscosities is $CEt_2Me > CEtMe_2 > CPr^nMe_2 > CMe_3$ for either

FIG. 2.

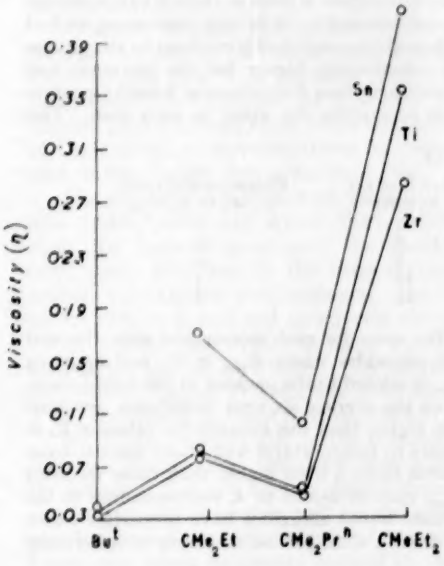
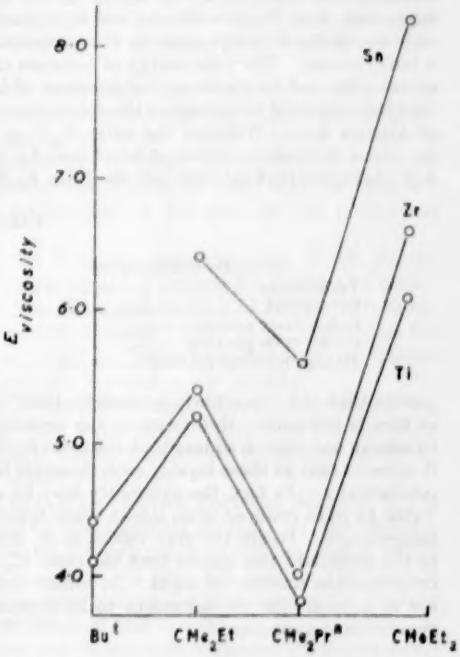



FIG. 3.




titanium or zirconium alkoxides. In the case of tin the order is the same but for the absence of data on the tertiary butoxide. The abnormal behaviour of the derivatives of 2-methylpentan-2-ol (dimethyl-*n*-propylcarbinol) is shown in Fig. 2. In Fig. 3 it is seen that the abnormality is also present in the values of $E_{visc.}$. The trend in positive entropy of activation is very similar. There is no doubt that these alkoxides are monomeric and that the behaviour is not due to metal–oxygen intermolecular bonding of the type involved in the complex normal alkoxides. Moreover, it is clear that the order of viscosities and of activation energies of viscosity $CEt_2Me > CEtMe_2 > CMe_3$ is that to be expected on the basis of molecular size. Finally, it has been found that the energies of cohesion for the derivatives of 3-methylpentan-3-ol and 2-methylpentan-2-ol (diethylmethyl- and dimethyl-*n*-propyl-carbinol) are quite close, and the inescapable conclusion is that the abnormal viscosity behaviour is caused by the abnormally low activation energy of viscosity. The possibility then arises that perhaps the mechanism of viscous flow is different for the derivatives of 2-methylpentan-2-ol from those of the other metal alkoxides. It has been implied throughout that the simple molecule is the unit of flow, but it appears that a smaller unit of flow may obtain for derivatives of this alcohol. This idea is not without precedent, since Eyring suggests that in long-chain hydrocarbons the unit

of flow is a segment of the simple molecule. In pictorial terms this means that viscous flow in the long molecules occurs by a mode of molecular " wriggling " rather than by molecular jumps.

Grunberg and Nissan [3] have also considered the structure of liquids by comparing the energies of vaporisation, viscosity, and cohesion. They found that for non-polar substances the activation energy of viscosity $E_{visc.}$ was equal to the energy of cohesion $W_c$. For polar associated liquids they found that $E_{visc.} > W_c$ and regarded the difference between these terms as a measure of the energy of dissociation. Moreover, with the aid of some assumptions concerning the number of intermolecular " bonds " broken in surface formation and in vaporisation, they suggested that the ratio $E_v/W_c$ or $E_v/E_{visc.}$ for non-polar liquids is related to the " statistical structure " of the liquid as shown in Table 13.

It is clear from Table 11 that, with the exception of complex titanium *n*-alkoxides and the titanium and zirconium derivatives of 2-methylpentan-2-ol, the values are in good agreement. With regard to the complex titanium *n*-alkoxides, it is seen that the activation energies of viscosity are considerably in excess of the energies of cohesion, which confirms the early suggestion that these molecules are depolymerised before engaging in viscous flow. This is well shown by a comparison of the monomeric *tert.*-butoxide of titanium with its complex *n*-butyl isomer. Thus the energy of cohesion of the *n*-butoxide is close to the activation energy of viscosity and to the energy of cohesion of the *tert.*-butoxide. It is very interesting to find that the abnormal behaviour of the derivatives of 2-methylpentan-2-ol is confined to the process of viscous flow. Whereas the ratio $E_v/E_{visc.}$ is considerably higher for the titanium and zirconium derivatives of this carbinol than for the corresponding derivatives of 3-methylpentan-3-ol (diethylmethylcarbinol) yet the ratio $E_v/W_c$ is practically the same in each case. This

TABLE 13.

| Molecular configuration | Co-ordination number | Characteristic ratio, $E_v/W_c$ or $E_v/E_{visc.}$ |
|---|---|---|
| Tetrahedral | 4 | 2 |
| Octahedral | 6 | 3 |
| Cubic, body-centred | 8 | 4 |
| Cubic, close packing | 12 | 4 |
| Hexagonal close packing | 12 | 4 |

proves that the " equilibrium configuration " is the same for each isomer and only the unit of flow is different. Returning to the monomeric alkoxides where $E_{visc.} \simeq W_c$ and applying Grunberg and Nissan's ideas that the ratio $E_v/E_{visc.}$ is related to the packing in the liquid state, it appears that in these liquids each molecule has on the average six near neighbours arranged octahedrally. In fact, the symmetry may be even higher than this because the values of $E_v$ in Table 13 were deduced from latent heats appropriate to temperatures well above normal room temperature. Hence the true values of $E_v$ are liable to be a little higher than those recorded in the table and this means that the ratio $E_v/E_{visc.}$ may be nearer to 4, corresponding to the co-ordination number of eight. In either case these liquid alkoxides have properties which are in accord with the behaviour to be expected from a close-packed assembly of spherically symmetrical molecules.

I have an uncomfortable feeling that I have stirred up far more questions than I have answered. I suppose this must always be the case when one seeks to explore fundamental principles. Indeed, I doubt if any fundamental principles are susceptible of precise formulation.

There are many voices raised today to impress on us the importance, the prime importance, of chemistry to industry, agriculture, medicine, and defence. It is most desirable that this should be said and said often. There is a real danger, however, that the practical applications of chemistry rather than its theoretical principles and fundamental discoveries should be uppermost in our esteem. Perhaps this is traditional. Alchemy was a very utilitarian pursuit of the elixir of life, whereby age and death might be defeated, and of the " philosopher's stone " which would transmute the elements into gold. No one can say what useful practical device may ultimately come from discoveries made purely in the pursuit of knowledge. Applied science draws its life-blood from pure science. Although we may be fascinated by applied science it must never weaken our allegiance to pure science.

[3] Grunberg and Nissan, *Trans. Faraday Soc.*, 1949, **45**, 125.

# ONE HUNDRED AND FIFTEENTH ANNUAL GENERAL MEETING.

THE One Hundred and Fifteenth Annual General Meeting of the Chemical Society was held in the Great Hall of The University, Nottingham, on Tuesday, March 27th, 1956, the President, Professor W. Wardlaw, being in the Chair. The Notice convening the Meeting was read by Professor E. D. Hughes, Honorary Secretary, who was invited by the President to present the Report of Council for the year ended December 31st, 1955.

Professor Hughes referred to the new subscription arrangements, which had been generally welcomed, and their effect on the Fellowship. Although a number of resignations had been received when the arrangements were introduced, this trend had now been reversed, and the Council was actively considering means whereby the Fellowship could be further increased.

Professor Hughes referred also to the many activities of the Society recorded in the Report of Council, and mentioned especially the honours conferred upon Fellows in the Birthday and New Year Honours Lists, and the award of the Nobel Prize for Chemistry to Professor du Vigneaud, an Honorary Fellow of the Society. In conclusion, Professor Hughes paid a tribute to all those who had assisted the Society in many ways as Members of Committees or representatives on various bodies, and to the work of the permanent staff of the Society during the past year.

The Accounts for 1955 were presented by the Honorary Treasurer, Mr. M. W. Perrin, who referred to the new layout which he hoped would make it simpler for Fellows to understand the financial position of the Society. The Financial Section of the Report, moreover, drew attention to the main features of the Accounts and, in particular, to the revised subscription arrangements. So far as could be judged on the basis of limited experience, these had had no adverse effect upon the finances of the Society.

Mr. Perrin referred also to plans which the Council had lately approved for improving further the service to Fellows. In particular, the *Proceedings*, which was the Society's only link with many Fellows, was to be increased in size and, he hoped, made more readable. A full statement on these proposals would be issued to Fellows.

Mr. Perrin referred also to the transfer of £5,000 on General Purposes Account to the Society's reserve, and welcomed this addition to the financial strength of the Society. He indicated that the surplus should in part be set against previous deficits, and it would also be required to meet in part capital expenditure over the next few years. The Council had, for example, recently approved proposals for refurnishing and rearranging the Meeting Room, and would be greatly assisted by the existence of this surplus.

Turning to the cost of publications, Mr. Perrin mentioned with appreciation the financial assistance received from the Chemical Council. It had been found necessary to make certain increases in the price at which publications were sold to non-Fellows. He was, however, pleased to report that the Council had agreed that no changes be made in the price of publications to Fellows for 1957. There would be no increase in costs, therefore, for Fellows before January 1st, 1958, at the earliest.

After discussion the President moved that the Report of Council and the Accounts for 1955 be adopted by the Meeting. This proposal was seconded by Dr. L. E. Sutton, Honorary Secretary, and was agreed unanimously.

The President then reported the following elections to the Council :

*President :*

Professor E. L. Hirst.

*Honorary Secretary :*

Dr. J. Chatt.

*Vice-Presidents who have not filled the Office of President:*

Professor E. D. Hughes.

*Elected Ordinary Members of Council:*

*Constituency I:*

Professor R. M. Barrer.
Dr. G. W. Kenner.
Dr. A. Maccoll.
Mr. L. A. K. Staveley.

*Constituency II:*

Professor A. G. Evans.

*Constituency IV:*

Professor L. Hunter.
Professor B. Lythgoe.

On the motion of the Honorary Treasurer, seconded by Professor F. Bergel, Messrs. W. B. Keen and Co., Finsbury Circus House, London, E.C.2., were reappointed as the Society's Auditors for 1956.

A vote of thanks to the President, Officers, Council and Local Representatives was proposed by Professor A. W. Johnson, and was carried with acclamation.

After an interval, the Meeting was resumed at 10.45 a.m., and the President presented the Corday–Morgan Medal and Prize for 1954 to Dr. R. E. Richards.

Professor Wardlaw then delivered his Presidential Address "Alkoxides, Old and New."

A vote of thanks to the President for his address was proposed by Professor H. W. Melville, and was carried with acclamation.

At the conclusion of the Meeting the President referred briefly to his pleasure in serving the Society as President during the past two years, and in handing over the badge of office to his old colleague and friend, Professor E. L. Hirst. Professor Hirst, in a brief reply, expressed his appreciation of the honour accorded to him by the Society.

# REPORT OF COUNCIL FOR 1955.

## I. FELLOWSHIP.

1. *General.* On December 31st, 1955, the number of Fellows of the Society was 8936. Fellowship changes during 1955 and previous years are given in the following Table :

TABLE I.

| | 1951. | 1952. | 1953. | 1954. | 1955. |
|---|---|---|---|---|---|
| Number of Fellows on January 1st | 8353 | 8616 | 9063 | 9249 | 9123 |
| *Additions :* | | | | | |
| Elections | 700 | 947 | 790 | 670 | 678 |
| Reinstatements | 25 | 34 | 29 | 26 | 27 |
| Miscellaneous | — | 1 | — | — | — |
| | 725 | 982 | 819 | 696 | 705 |
| *Deductions :* | | | | | |
| Deaths | 62 | 65 | 58 | 71 | 60 |
| Resignations | 273 | 341 | 467 | 583 | 712 |
| Removals | 127 | 128 | 106 | 167 | 117 |
| Miscellaneous | — | 1 | 2 | 1 | 3 |
| | 462 | 535 | 633 | 822 | 892 |
| Net change in year | +263 | +447 | +186 | −126 | −187 |

At the end of 1954 and in the early months of 1955, following the cessation of the Joint Subscription Scheme, a large number of resignations were received. However, resignations at the end of 1955 were substantially fewer, and the Council is actively considering means whereby this trend can be maintained and the Fellowship increased.

2. *Congratulations.* The congratulations of the Society were conveyed to the following Fellows who were honoured in the Birthday and New Year Honours Lists :

*K.B.E.*
Alexander Fleck.
Owen Haddon Wansbrough-Jones.

*C.B.*
Norman Charles Wright.

The Council has congratulated Professor Vincent du Vigneaud (Honorary Fellow) on the award of the Nobel Prize for Chemistry, and also the following, who received awards announced by the Royal Society :

*Royal Medal.*
Sir Alexander Todd.

*Davy Medal.*
Professor H. W. Melville.

## II. PUBLICATIONS.

1. *Journal.* During 1955, 1084 scientific communications were received for publication in the *Journal*, this number being an increase of 6·3% over that (1019) received during 1954 and a record for any year in the Society's history. Some comparative figures on this and other aspects of publications in the *Journal* are given in Tables 2—6.

TABLE 2.

| | 1938. | 1952. | 1953. | 1954. | 1955. |
|---|---|---|---|---|---|
| Papers and Notes received | 507 | 1046 | 946 | 1019 | 1084 |
| *Less* rejected or withdrawn | 11 | 59 | 52 | 49 | 68 |
| | 496 | 987 | 894 | 970 | 1016 |
| Papers and Notes published | 404 | 1000 | 866 | 961 | 908 |
| No. of pages (Papers and Notes) | 1917 | 4901 | 4028 | 4552 | 4297 |
| No. of pages (total, excluding Index Volume) | 2120 | 5056 | 4200 | 4712 | 4496 |
| Average no. of pages per communication | 4·75 | 4·90 | 4·65 | 4·73 | 4·73 |

TABLE 3.

*Numbers of Communications Received for Publication.*

| Year | 1938 | 1944 | 1947 | 1948 | 1949 | 1950 | 1951 | 1952 | 1953 | 1954 | 1955 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Nos. | 507 | 242 | 523 | 548 | 739 | 874 | 910 | 1046 | 946 | 1019 | 1084 |

TABLE 4.

*Numbers of Items in the* Journal.

| | 1938. | 1948. | 1952. | 1953. | 1954. | 1955. |
|---|---|---|---|---|---|---|
| Papers (General, Physical, and Inorganic) | 102 | 124 | 194 | 180 | 135 | 168 |
| ,, (Physical Organic) | — | 16 * | 134 | 93 | 125 | 153 |
| ,, (Organic) | 275 | 326 | 556 | 492 | 581 | 474 |
| Notes | 27 | 45 | 116 | 101 | 120 | 113 |
| Lectures and Addresses | 9 | 5 | 6 | 6 | 7 | 4 |
| Obituary Notices | 37 | 17 | 21 | 14 | 22 | 12 |
| Annual General Meeting | 1 | 2 | 2 | 1 | 1 | 1 |
| Extraordinary General Meeting | — | — | — | — | 1 | — |
| Bye-laws of the Chemical Society | — | — | — | — | 1 | — |
| Editorial Nomenclature Report | — | — | 1 | 1 | 1 | 1 |
| I.U.P.A.C. List of Atomic Wts. | 1 | — | — | 1 | 1 | — |
| | 452 | 535 | 1030 | 889 | 995 | 926 |

* Class first introduced December 1948.

TABLE 5.

*Percentage Distribution in the* Journal.

| | 1948. | 1949. | 1952. | 1953. | 1954. | 1955. |
|---|---|---|---|---|---|---|
| Papers (General, Physical, and Inorganic) | 20·3 | 16·9 | 19·4 | 20·8 | 14·0 | 18·5 |
| ,, (Physical Organic) * | 3·1 | 14·4 | 13·4 | 10·8 | 13·0 | 16·9 |
| ,, (Organic) | 63·8 | 60·9 | 55·6 | 56·7 | 60·5 | 52·2 |
| Notes | 8·8 | 7·8 | 11·6 | 11·7 | 12·5 | 12·4 |

* Class first introduced December 1948.

Communications published in the *Journal* during 1955 numbered 908, a decrease of 5·6% compared with the number (961) published during 1954. This decrease was due to difficulties at the printers, and steps have been taken which it is hoped will overcome the difficulties and permit the arrears to be soon overhauled.

Contributions from industrial laboratories and industrial research organisations published during 1955 totalled 94, including 7 published jointly with academic institutions and 1 jointly with a Government organisation; this represents 10·3% of the total (the figure for 1954 was 13·1%). Contributions from Government sources totalled 43, 4·7% (1954, 4·9%), including 10 jointly with academic institutions and 1 jointly with an industrial organisation. Contributions from overseas published during 1955 numbered 166 (18·3%) (1953, 16·2%;

TABLE 6.

| | 1948. | 1952. | 1953. | 1954. | 1955. |
|---|---|---|---|---|---|
| Australia | 13 | 62(1) | 50 | 62(2) | 46(2) * |
| British Colonies and Protectorates | — | 6(3) | 5(1) | 9(2) | 7 |
| Canada | 2 | 2(1) | 2 | 6(1) | 12(4) † |
| Egypt | 15 | 12 | 8 | 16 | 15 |
| France | 2 | 10 | 7 | 8(2) | 10 |
| Hungary | 6 | 3 | 7 | — | 4 |
| India and Pakistan | 3 | 3(1) | 6 | 13 | 15 |
| Irish Republic | — | 4 | 5 | 5 | 10(2) |
| Israel | 2 | 10(2) | 20 | 15 | 11(1) |
| Italy | — | — | — | 9 | 1 |
| Japan | — | — | — | — | 5 † |
| New Zealand | 14 | 18 | 12(1) | 14(1) | 10 |
| South Africa | 1 | 14(1) | 7 | 8(1) | 9 |
| U.S.A. | 2 | 8(3) | 7(1) | 24(3) | 7(1) * |
| Miscellaneous | 7 | 5 | 4(1) | 5(1) | 8(2) |
| | 67 | 157(12) | 140(4) | 194(13) | 166(12) |

* Includes 1 jointly. † Includes 3 jointly.

1954, 20·2%). These sources therefore do not account for the increased receipts during 1955. In Table 6 joint publication is shown in parentheses.

2. *Annual Reports on the Progress of Chemistry for* 1954 (*Volume LI*). These were issued in July 1955 and contained 400 pages (378 in 1954).

3. *Quarterly Reviews.* Volume IX (1955) contained 15 articles occupying 414 pages (Volume VIII, 17 articles, 450 pages). A Cumulative Index of Authors and a short Cumulative Index of Subjects was included at the end of the volume, as in 1954.

4. *Current Chemical Papers.* In its second year, *Current Chemical Papers* was produced essentially on the same lines as in the previous year. However, the classification used for physical chemistry was revised so as to bring closer together papers in specific fields of work.

The number of journals covered was increased during the year from 437 to 469, and there was an increase (11½%) in the number of pages of *Current Chemical Papers*. Coverage is believed to be now fairly comprehensive for pure chemistry, except for Russian regional journals, of which few were delivered during 1955 (it is hoped that this situation will improve in 1956); lists of journals covered are published with the January issues (1955 and 1956), and suggestions to the Editor for additional journals will be welcome.

An edition on air-mail paper and an edition printed only on one side of the paper were available in 1955.

Comparative statistics are given in Tables 7—9. Apart from the overall increase in size, differences between the figures for 1954 and 1955 do not seem to be significant.

5. *Special Publications.* Special Publication No. 2, *a Report of a Symposium on "Peptide Chemistry,"* held in London on March 30th, 1955, was published in July, 1955. Special Publication No. 3, *a Report of a Symposium on "Recent Work on Naturally Occurring Nitrogen Heterocyclic Compounds,"* held in Exeter on July 13th—15th, 1955, was published in January, 1956.

TABLE 7.

Current Chemical Papers: *Summary.*

| | Totals. | | Average per issue. | |
|---|---|---|---|---|
| | 1954. | 1955. | 1954. | 1955. |
| Titles of papers listed | 19,531 | 21,360 | 1628 | 1780 |
| Issues of journals yielding titles | 2006 | 2277 | 167 | 190 |
| Journals yielding titles | 325 | 381 | 129 | 182 |
| Pages (of *C.C.P.*) | 633 | 706 | 53 | 58 |
| Issues of journals not yielding titles | — | 1438 | 137 | 120 |
| Total number of journals scanned | 437 | 469 | — | — |

TABLE 8.

*Papers in* Current Chemical Papers, *classified according to the Country in which the original Journal was published.*

| | Numbers. | | Percentages. | | No. of journals. |
|---|---|---|---|---|---|
| | 1954. | 1955. | 1954. | 1955. | 1955. |
| U.S.A. | 6104 | 6356 | 32·54 | 29·77 | 66 |
| U.K. | 2625 | 3126 | 13·94 | 14·63 | 66 |
| Germany | 1889 | 2111 | 10·02 | 9·88 | 36 |
| U.S.S.R. | 1760 | 2037 | 9·35 | 9·54 | 15 |
| Japan * | 1653 | 1691 | 8·78 | 7·92 | 38 |
| France | 1113 | 1205 | 5·91 | 5·64 | 21 |
| Scandinavia | 494 | 757 | 2·62 | 3·54 | 21 |
| India | 443 | 611 | 2·35 | 2·86 | 17 |
| Czechoslovakia * | 328 | 591 | 1·74 | 2·77 | 4 |
| Netherlands | 509 | 585 | 2·70 | 2·74 | 10 |
| British Commonwealth (other than U.K. and India) | 311 | 423 | 1·65 | 1·98 | 19 |
| Italy | 393 | 385 | 2·09 | 1·80 | 13 |
| Switzerland | 297 | 325 | 1·58 | 1·52 | 7 |
| Poland | 166 | 261 | 0·89 | 1·22 | 3 |
| Austria | 81 | 251 | 0·43 | 1·18 | 5 |
| Hungary | 174 | 159 | 0·93 | 0·74 | 5 |
| Spain and Portugal | 257 | 155 | 1·37 | 0·73 | 8 |
| Jugoslavia | 94 | 93 | 0·50 | 0·44 | 4 |
| Belgium | 45 | 84 | 0·24 | 0·39 | 5 |
| Latin America | 50 | 71 | 0·27 | 0·33 | 10 |
| China (Formosa) | — | 31 | — | 0·14 | 1 |
| Roumania | — | 30 | — | 0·14 | 3 |
| Israel | 8 | 11 | 0·04 | 0·05 | 1 |
| Turkey | 12 | 11 | 0·06 | 0·05 | 3 |
| | 18,806 | 21,360 | 100·00 | 100·00 | 381 |

* Too high owing to duplicate publication in Japanese or Czech and other languages.

TABLE 9.

*Languages used in Papers included in* Current Chemical Papers—*Approximate Percentages.*

| | 1954. | 1955. |
|---|---|---|
| English | 59·5 | 56·8 |
| German | 13·2 | 13·9 |
| Russian | 9·4 | 9·9 |
| French | 7·1 | 6·6 |
| Japanese | 4·4 | 6·2 |
| Italian | 2·1 | 1·8 |
| Czech | 0·9 | 1·7 |
| Spanish and Portuguese | 1·6 | 1·0 |
| Polish | 0·5 | 1·0 |
| Hungarian | 0·5 | 0·3 |
| Others | 0·8 | 0·8 |
| | 100·0 | 100·0 |

## III. MEETINGS.

1. *Scientific Meetings.* Details of Scientific Meetings held in London and those arranged at various centres by Local Representatives of the Society are given in Appendix A.

2. *Anniversary Meetings.* The Anniversary Meetings were held in London on March 30th and 31st and April 1st.

3. *Centenary Lectures.* Professor H. C. Brown (Purdue University, Indiana), delivered a Centenary Lecture, entitled " Chemical Effects of Steric Strains " in London, Leeds, Manchester, Newcastle upon Tyne, and Sheffield. Professor M. Calvin (University of

California, Berkeley) delivered a Centenary Lecture entitled " The Photosynthetic Carbon Cycle " at London, Glasgow, Manchester, and Birmingham.

## IV. LIBRARY.

A major programme of modernisation and improvement has been undertaken in the Library. The space available for readers has been increased and new furniture installed. Additional storage accommodation has been secured outside Burlington House for those books and periodicals that are in less frequent demand. These changes are referred to in greater detail in the Report of the Joint Library Committee (Appendix B).

## V. OTHER ACTIVITIES.

1. *Grants for Research.* Grants from the Research Fund totalling £668 were made to twenty-five applicants.

2. *Corday–Morgan Medal and Prize.* The Corday–Morgan Medal and Prize for 1953 was awarded to Dr. J. W. Cornforth.

3. *Third International Congress of Biochemistry.* Professor F. Bergel represented the Society at this Conference in Brussels.

4. *International Conference on Co-ordination Compounds.* Dr. L. E. Sutton represented the Society at this Conference in Amsterdam.

5. *German Chemical Society.* Professor E. D. Hughes and Mr. J. R. Ruck Keene attended the Annual Meetings held in Munich from the 11th—16th September, 1955.

## VI. ADMINISTRATION.

1. *Council.* At the Annual General Meeting on April 1st, the following were elected :

| | |
|---|---|
| Honorary Secretary ..... | Professor F. Bergel. |
| Vice-Presidents who have not filled the Office of President ..... | Professor M. Stacey, Sir Alexander Todd. |
| Elected Ordinary Members of Council..... | Dr. D. W. Adamson, Dr. G. R. Barker, Professor F. Bell, Dr. A. Hickling, Dr. A. W. Johnson, Dr. A. Maccoll, Dr. F. H. Pollard, Dr. W. Wild, Dr. G. T. Young. |

2. *Local Representatives.* The following changes in appointments have been made :

| | |
|---|---|
| Australia..... | Dr. K. H. Pausacker in place of Professor A. J. Birch. |
| Canada ..... | Professor J. K. N. Jones in place of Dr. D. W. McFarlane. |
| Edinburgh ..... | Dr. G. O. Aspinall in place of Dr. T. R. Bolam. |
| India ..... | Professor T. R. Seshadri in place of Sir Shanti Bhatnagar. |
| Manchester..... | Mr. A. C. Farthing in place of Dr. M. A. T. Rogers. |
| South Africa ..... | Professor F. L. Warren in place of Professor W. Pugh. |

3. *Administrative Offices.* As part of a scheme for providing improved accommodation for the Library, certain members of the Society's administrative staff are now housed at 9/10 Savile Row, and the main stock of the Society's publications has been moved there. Arrangements have also been made for the editorial staff to transfer to Savile Row at a later date. All communications from Fellows, however, should still be sent to Burlington House, which remains the postal address of the Society.

## VII. FINANCE.

1. *Method of Presentation of the Accounts.* The Council hopes that Fellows will find the new lay-out of the Accounts, made possible largely as a result of the revised subscription arrangements, more simple than that adopted in former years. However, since individual items are, in some cases, compiled on a different basis, it is not possible to show comparative figures for the preceding year.

Whereas formerly all the expenses of publication were included in the Publications Account, the income shown there was only that received from non-Fellows, from advertisement revenue, and from the Publications Fund investments. The income received from Fellows for publications supplied was included with subscription income, and was shown in the General Purposes Account. Now all income from publications, from whatever source it is received, is shown in the Publications Account. The accounts for 1955, therefore, indicate for the first time the true financial position of each of the Society's main publications.

For greater clarity the Publications Fund and the Special Reserve Fund have been consolidated with the General Purposes Fund in one Balance Sheet. The Special Publications Fund and the Staff Pensions Fund are also included, although separate income and expenditure accounts are given, and the exact position of each fund and its investments is still shown separately, in the Assets side of the Balance Sheet.

The Trust Funds which the Society administers are now, for convenience, collated into one Balance Sheet, although separate Income and Expenditure Accounts are still shown.

2. *Revised Subscription Arrangements.* The period under review is the first year in which the Fellowship subscription has been reduced to two guineas. The Council was of the opinion that the adoption of this arrangement, whereby it was no longer obligatory for Fellows to pay for publications unless they wished to receive them, would not adversely affect the net financial position of the Society. Furthermore, it was hoped that the loss of Fellows by resignation would be reduced, and thus the subscription income of the Society might gradually increase. This in turn would cover further rises in costs or, alternatively, would help in any expansion of the Society's activities.

So far as can be judged on the basis of only one year's experience, it can be reported that the Council's hopes regarding the effect of the new arrangements on the finances of the Society have been realised. The total receipts from Fellows for subscriptions and publications amounted to £37,279 in 1954. In 1955 the income from Fellows amounted to £34,510, of which £17,019 was received by way of subscriptions, and a further £17,491 was received as payment for publications, thus showing a decrease of £2769. Against this decrease should be set a saving of not less than £1800 through the reduced circulation to Fellows of publications, and a further saving of some £1000 in administrative costs that arises from the closing of the Conjoint Chemical Office.

The General Purposes Account shows an excess of income over expenditure of £246 after £5,000 has been transferred to General Reserve. This is not unexpected in the first year of the new subscription arrangements now that income and expenditure relating to publications are separated from that attributable to other activities. The surplus should in part be offset against previous deficits or losses incurred by the depreciation in the value of investments. Moreover, some of this reserve will probably be required to meet capital expenditure which the Society is likely to incur over the next few years, and which should not be deferred. Whilst the surplus is likely to be considerably smaller in the future, and, indeed, may become a deficit if costs continue to rise faster than income, it does strengthen the Council's opinion that the present rate of annual subscription can, subject to factors outside the Society's control, be stabilized in an inflationary period. The Council, by practising all reasonable economies, and by maintaining an efficient administration, intends to avoid, so far as lies within its power, the necessity for any increase in the Fellows' subscription.

3. *Cost of Publications.* The Publications Account shows how large a proportion of the Society's resources is devoted to publications, and, especially, to the *Journal*.

Had it not been for the difficulties in the printing industry which have restricted the size of the *Journal*, the cost of this item would have been even higher and the Publications Account would not have shown an excess of income over expenditure. The number of papers awaiting publication has been increasing now for the past two years, and amounts to the equivalent of some 400—500 *Journal* pages, or £3500—£4500 in terms of publication costs. The Council hopes that the difficulties of production will be overcome, although it will inevitably take some time to eliminate entirely the arrears. The cost will, unfortunately, have to be met at the much increased prices now prevailing.

For several years now, and before the new subscription arrangements were introduced, individual Fellows have tended to discontinue subscriptions to the *Journal*, and to rely on copies from libraries. The trend still continues (see Table 10).

TABLE 10.

*Circulation of the* Journal.

| | | Nos. circulated in year of publication. | | |
|---|---|---|---|---|
| | Nos. printed.* | Fellows. | Non-Fellows. | Exchanges. |
| 1947 | 6425 | 4340 | 1357 | 80 |
| 1948 | 6300 | 4317 | 1547 | 80 |
| 1949 | 6800 | 4472 | 1627 | 80 |
| 1950 | 7000 | 4337 | 1684 | 80 |
| 1951 | 7000 | 4442 | 1989 | 80 |
| 1952 | 7500 | 4795 | 2095 | 80 |
| 1953 | 7000 | 3936 | 2273 | 88 |
| 1954 | 6900 | 3761 | 2359 | 90 |
| 1955 | 6400 | 3243 | 2521 | 90 |

* The difference between the number printed in any year and the number circulated in that year represents the stock available as replacements, or to supply the demand for back numbers.

The falling circulation of the *Journal* among Fellows has not materially affected the Society's finances, since Fellows can obtain copies at approximately the " run-on " cost of paper, printing, and distribution. The increased circulation to non-members has, on the other hand, been of considerable benefit. In spite of this increase, however, the Publications Account would have shown a deficit had it not been for a grant of £5500 received from the Chemical Council. The Council wishes to record its grateful thanks to the Chemical Council, and to industry for this assistance.

4. *Improvements at Burlington House and* 9/10 *Savile Row.* The cost of the improvements to the Library, and to the offices at 9/10 Savile Row for the administrative and editorial staff, is shown in the Accounts. The improvements to the Library were made possible by a grant of £10,000 from the Chemical Council. The Council has recorded its warm and appreciative thanks to the Chemical Council for this generous contribution.

5. *Investments.* Investments on General Purposes Account include £4305 19*s.* 4*d.* received in 1954 from the A. G. Perkin Bequest, invested in 1955, and a further investment of £1500 made on the Centenary Fund. These, and other smaller changes, are included in the Schedules at the end of the Accounts.

6. *Staff.* The Council has approved new salary scales for the Society's staff, which took effect on January 1st, 1956. These scales recognise the substantial rise in the cost of living that has taken place since the previous comprehensive review of salaries and salary scales.

The Staff Superannuation Scheme has also been reviewed, and new and improved arrangements have been introduced which will give considerably improved retirement benefits to the permanent staff of the Society at a very small extra cost.

## VIII. REPRESENTATIVES OF THE SOCIETY ON OTHER BODIES.

In 1955 the Society was represented on various bodies by as follows :

*" Acta Metallurgica " :*

International Journal of the Science of Metals : Dr. U. R. Evans.

*Barker Committee :*

Formed to support the publication of the Barker Index of the characteristic angles of crystalline compounds : Dr. G. M. Bennett.

*Bristol University Court :*

Professor C. E. H. Bawn.

*British National Committee for Biochemistry :*

Professor F. Bergel, Professor M. Stacey.

*British National Committee for Chemistry :*

Sir Eric Rideal, Professor E. D. Hughes, Mr. M. W. Perrin.

*British National Committee for Crystallography :*

Professor J. M. Robertson.

*British Standards Institution. Technical Committees :*

| | |
|---|---|
| C/17. | Viscosity : Dr. A. E. Dunstan. |
| C/34. | Standardization of pH Scale : Professor H. T. S. Britton. |
| CHE/36. | Chemicals and Chemical Plant for Electroplating : Dr. J. R. I. Hepburn. |
| DAC/-. | Dairying Industry Standards Committee : Mr. Eric Voelker. |
| FCC/HCC/1. | Nomenclature for Fine and Heavy Chemicals Industries : The Editor. |
| HCC/2. | Desiccants : Dr. B. Lambert. |
| LBC/-. | Scientific Glassware and Related Laboratory Apparatus, Industry Standards Committee : Dr. G. R. Davies. |
| LBC/1/1. | Dean and Stark and Ubbelohde Apparatus : Dr. G. R. Davies. |
| LBC/5. | Hydrometers : Mr. R. Sutcliffe. |
| LBC/6. | Standard Distillation Apparatus : Mr. R. Sutcliffe. |
| LBC/11. | Microchemical Apparatus : Dr. R. Belcher, Dr. H. D. K. Drew. |
| LBC/11/1. | Apparatus for Microchemical Combustion Methods : Dr. R. Belcher. |
| LBC/11/3. | Accessory Apparatus connected with Gravimetric microanalysis : Dr. R. Belcher. |
| LBC/16. | Glass Electrodes : Dr. D. J. G. Ives. |
| LBC/16/2. | Drafting Work on pH Meters : Dr. D. J. G. Ives. |
| LBC/17. | Laboratory Apparatus Drawing Conventions : The Editor. |
| LBC/18. | Laboratory Furniture and Fittings : Mr. R. Sutcliffe. |
| LGE/19. | Colour Terminology : Dr. F. M. Hamer. |
| PAC/13. | Filter Paper : Mr. F. H. Burstall. |
| PAC/13/1. | Laboratory Filter Paper (Drafting) : Mr. F. H. Burstall. |
| PCC/1. | Nomenclature for Pest Control Products : The Editor. |
| RUC/8. | Rubber Tubing and Bungs for Laboratory Use : Dr. L. C. Bateman. |
| USM/1. | Co-ordination of Definitions, Units and Technical Date : The Editor. |
| USM/1/8. | Glossary of Terms used in Nuclear Sciences : The Editor. |
| USM/2. | Abbreviations and Symbols : The Editor. |
| USM/2/2. | Abbreviations and Letter Symbols (Chemical Engineering and Applied Chemistry Sub-Committee) : The Editor. |

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## APPENDIX A.

### MEETINGS HELD DURING 1955.

### IN LONDON.

(Meetings were held in the Rooms of the Society at Burlington House unless otherwise stated.)

January 20th at the Imperial College of Science and Technology, *Tilden Lecture,* " The Rôle of the π-Electron in Aromatic Chemistry," by Professor H. C. Longuet-Higgins; February 3rd, *Meeting* for the reading of original papers; February 17th, *Meeting* for the reading of original papers; March 17th, *Pedler Lecture,* " Some Problems in the Chemistry of the Hemicelluloses," by Professor E. L. Hirst; May 5th, *Meeting* for the reading of original papers; June 2nd, *Centenary Lecture,* " Chemical Effects of Steric Strains," by Professor H. C. Brown; October 20th, at the Institution of Civil Engineers, *Centenary*

*Lecture*, " The Photosynthetic Carbon Cycle," by Professor M. Calvin; November 3rd, *Meeting* for the reading of original papers; November 17th, at the Imperial College of Science and Technology, *Tilden Lecture*, " Some Developments in the Study of Physical Adsorption," by Professor D. H. Everett; December 1st, at the Royal Institution, *Liversidge Lecture*, " Reactions of Radicals in Gaseous Systems," by Dr. E. W. R. Steacie; December 15th, *Meeting* for the reading of original papers.

**OUTSIDE LONDON**

*Aberdeen.* Joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry, at Robert Gordon's Technical College, unless otherwise stated: January 13th, *Lecture*, " Application of Science in the Detection of Crime," by Dr. J. B. Firth; February 25th, *Lecture*, " Corrosion Processes: their Causes and Prevention," by Dr. F. Wormwell; March 17th, *Lecture*, " Fluorescence of Solutions," by Dr. E. J. Bowen; October 28th, at Marischal College, *Lecture*, " Electron-transfer Reactions," by Professor C. E. H. Bawn; November 24th, in the University Chemistry Department, Old Aberdeen, *Liversidge Lecture*, " Reactions of Radicals in Gaseous Systems," by Dr. E. W. R. Steacie; December 9th, at Marischal College, *Lecture*, " Some Chemical Aspects of Cell Structure," by Professor J. N. Davidson.

*Birmingham.* At the University: January 14th, joint meeting with Birmingham University Chemical Society, *Lecture*, " The Structures of Electron-deficient Substances," by Professor H. C. Longuet-Higgins; February 4th, *Official Meeting and Lecture*, " The Photochemistry of Polymethyl Vinyl Ketone," by Professor R. G. W. Norrish; March 4th, joint meeting with Birmingham University Chemical Society, *Lecture*, " Ionisation in Organic Chemistry," by Professor E. D. Hughes; October 14th, joint meeting with Birmingham University Chemical Society, *Lecture*, " New Aspects of Aromatic Character," by Professor Wilson Baker; October 24th, *Centenary Lecture*, " The Photosynthetic Carbon Cycle," by Professor M. Calvin; November 18th, joint meeting with Birmingham University Chemical Society, *Lecture*, " The Interpretation of Electromotive-force Measurements with Special Reference to the Gastric Mucosa," by Dr. A. G. Ogston.

*Bristol.* Joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry, at the University, unless otherwise stated: January 13th, *Lecture*, " Some Experiences of Food Legislation during the War," by Sir Harry Jephcott; January 27th, also joint with the Society for Analytical Chemistry, *Lecture*, " Recent Advances in the Bacteriological Examination of Water," by Dr. Windle Taylor; February 10th, *The Hugo Müller Lecture*, " Some Newer Aspects of the Organic Chemistry of Nitrogen," by Professor G. R. Clemo; February 17th, at The College of Technology, Gloucester, *Lecture*, " New By-products from Coal," by Dr. W. Idris Jones; March 3rd, also joint with the Institute of Fuel, *Lecture*, " The Fuel Scientist: Training and Using Britain's Greatest Asset," by Professor A. L. Roberts; March 17th, *Lecture*, " Some Recent Advances in Photography, by Dr. H. Baines; July 19th, also joint with the University Chemical Society, *Lecture*, " Organometallic Compounds of the Acetylenic Type," by Professor Dr. H. Hartmann; October 6th, *Lecture*, " The Impact of Nuclear Energy on Industry," by Dr. J. M. Fletcher; October 19th, at The Technical College, Gloucester, *Lecture*, " Some New Plastic Materials," by Dr. E. M. Evans; October 20th, *Lecture*, " Organic Inclusion Compounds and their Uses," by Professor Wilson Baker; October 27th, also joint with the University Chemical Society, *Lecture*, " Some Properties of Aqueous Hydrogen Fluoride Solutions," by Mr. R. P. Bell; November 3rd, *Lecture*, " New Aspects of the Chemistry of the Nitrogen Oxides," by Dr. C. C. Addison; November 10th, also joint with the University Chemical Society, *Lecture*, " The Problems Involved in Studying Fast Reactions," by Professor H. W. Melville; November 17th, *Lecture*, " Principles of Crystal Growth," by Professor F. C. Frank; November 24th, also joint with the University Chemical Society, *Lecture*, " The Scientific Examination of Paintings," by Dr. E. A. Werner; December 1st, also joint with the Institute of Metals, *Lecture*, " The Technology of Carbon and Graphite," by Mr. J. M. Hutcheon.

*Cambridge.* Joint meetings with the University Chemical Society, at the Chemical

Laboratory, Pembroke Street: January 21st, *Lecture*, "Recent Advances in Acetylene Chemistry," by Professor R. A. Raphael; January 28th, *Lecture*, "Topology and Chemistry," by Dr. A. F. Wells; February 18th, *Official Meeting and Lecture*, "The Physical Chemistry of Acetaldehyde Solutions," by Mr. R. P. Bell; May 11th, *Centenary Lecture*, "Chemical Effects of Steric Strain," by Professor H. C. Brown; October 21st, *Lecture*, "Homolytic Aromatic Substitution," by Professor D. H. Hey; November 4th, *Lecture*, "Synthetic Polypeptides," by Dr. C. H. Bamford; November 18th, *Lecture*, "Many-centre Bonds," by Professor H. C. Longuet-Higgins.

*Edinburgh.* Joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry, held at the North British Station Hotel, unless otherwise stated: January 13th, *Lecture*, "Organic Inclusion Compounds," by Professor W. Baker; February 1st, also joint with the University Chemical Society, at the Biochemistry Lecture Theatre, Teviot Place, *Lecture*, "The Foundation of Tyrosine Melanin," by Professor G. R. Clemo; February 24th, *Lecture*, "Mechanics of Droplets and Bubbles in Diffusion Processes," by Professor F. H. Garner; March 10th, *Lecture*, "The Changing Face of the Gas Industry," by Dr. A. Marsden; October 6th, *Society of Chemical Industry Lister Memorial Lecture*, "The Chemistry and Functions of Vitamin $B_{12}$," by Dr. E. Lester Smith; October 20th, *Lecture*, "Some Fatty Acids of Recent Description," by Dr. F. D. Gunstone; November 10th, *Lecture*, "Hydrogen-transfer Reactions," by Professor E. A. Braude; December 8th, *Lecture*, "Some Aspects of Research in the Scottish Division of the National Coal Board," by Dr. E. A. C. Chamberlain.

*Exeter.* At the Washington Singer Laboratories, unless otherwise stated: February 8th, *Lecture*, "The Chemistry of Melanin," by Professor G. R. Clemo; May 6th, *Lecture*, "Acetylene–Allene Chemistry," by Professor E. R. H. Jones; July 13th—July 15th, *Official Meeting and Symposium*, "Recent Work on Naturally Occurring Nitrogen Heterocyclic Compounds" (contributions from the following were read and discussed: Professor A. Albert, Professor J. Baddiley, Dr. A. R. Battersby, Dr. N. B. Chapman, Dr. J. Harley-Mason, Professor R. D. Haworth, Dr. A. W. Johnson, Professor R. P. Linstead, Dr. J. D. Loudon, Dr. S. F. Mason, Dr. H. T. Openshaw, Dr. T. S. Stevens, Sir Alexander Todd, and Dr. M. Whalley), October 28th, *Lecture*, "How Free are Free Radicals?" by Professor D. W. G. Style; November 25th, *Lecture*, "Homolytic Substitution Reactions," by Professor D. H. Hey.

*Glasgow.* February 18th, at the Royal Technical College, Annual General Meeting of local Fellows followed by a *Meeting* for the reading of original papers; March 18th, at the University, *Lecture*, "The Shape of Molecules," by Dr. J. W. Linnett; October 28th, at the University, *Official Meeting and Centenary Lecture*, "The Photosynthetic Carbon Cycle," by Professor M. Calvin; November 18th, at the University, *Lecture*, "Solid Imperfections and Chemical Reactivity," by Dr. F. C. Tompkins.

*Hull.* At the University: January 27th, *Lecture*, "Some Modern Ideas of the Nature of the Covalent Bond," by Professor C. A. Coulson; February 10th, *Lecture*, "Chromatography," by Dr. T. I. Williams; March 3rd, *Lecture*, "Some Recent Progress in Natural-product Chemistry," by Professor D. H. R. Barton; November 10th, *Lecture*, "Fast Reactions," by Professor G. Porter; November 24th, joint meeting with the Royal Institute of Chemistry, *Lecture*, "Direct Hydroxylation of Organic Compounds," by Professor W. Bradley.

*Irish Republic.* February 9th, at Trinity College, Dublin, *Tilden Lecture*, "The Rôle of the $\pi$-Electron in Aromatic Chemistry," by Professor H. C. Longuet-Higgins; March 4th, joint meeting with the Werner Society at Trinity College, Dublin, *Lecture*, "Organic Inclusion Compounds," by Professor W. Baker; March 23rd, at University College, Dublin, *Lecture*, "Recent Advances in Acetylene Chemistry," by Professor R. A. Raphael; May 9th, joint meeting with the Institute of Chemistry of Ireland, the Royal Institute of Chemistry, the Society of Chemical Industry, and University College, Dublin, at University College, Dublin, *Lecture*, "The Nature of Adsorption Forces," by Professor H. C. de Boer; May 10th, May 13th, and May 16th, joint meetings with the Institute of Chemistry of Ireland, the Royal Institute of Chemistry, and the Society of Chemical Industry, held at University College, Dublin, University College, Cork, and University College, Galway,

respectively, *Lecture*, " The Fundamental Principles of Catalysts," by Professor H. C. de Boer; May 20th, joint meeting with the Werner Society at Trinity College, Dublin, *Lecture*, " Some Applications of Flash Photolysis," by Professor R. G. W. Norrish; October 28th, joint meeting with the Werner Society at Trinity College, Dublin, *Lecture*, " Phenylation," by Professor D. H. Hey; November 30th, at Trinity College, Dublin, *Lecture*, " Properties of Periodate-oxidised Polysaccharides," by Dr. V. C. Barry.

*Leeds.* At the University: January 17th, joint meeting with the Royal Institute of Chemistry, *Lecture*, " Progress towards Atomic Power," by Dr. R. Spence; February 8th, *Lecture*, " Complexones," by Professor G. Schwarzenbach; February 21st, *Royal Institute of Chemistry Lecture*, " New Lamps for Old in Analytical Chemistry," by Dr. C. L. Wilson; March 10th, joint meeting with the University Chemical Society, *Lecture*, " Aphid Colouring Matters," by Sir Alexander Todd; March 14th, *Royal Institute of Chemistry Lecture*, " The Biochemistry of the Marine Algæ," by Dr. F. N. Woodward; May 18th, *Official Meeting and Symposium*, " The Friedel–Crafts Reaction " (contributions from the following were read and discussed: Dr. G. Baddeley, Professor W. Bradley, Professor H. C. Brown, Dr. R. O. Colclough, Professor A. G. Evans, Professor D. D. Eley, Dr. F. Fairbrother, Dr. D. C. Pepper, Professor P. H. Plesch, Dr. E. Rothstein); May 19th, *Centenary Lecture*, " Chemical Effects of Steric Strains," by Professor H. C. Brown; October 13th, joint meeting with the Royal Institute of Chemistry, the Society of Chemical Industry, the British Association of Chemists, and the University Chemical Society, *Lecture*, " The Mechanism of the Liquid-phase Oxidation of Decane," by Dr. G. H. Twigg; October 31st, *Lecture*, " The Hydrogen-isotope Effect in Reaction Kinetics," by Mr. R. P. Bell; November 7th, *Royal Institute of Chemistry Lecture*, " Antibiotics—Past, Present, and Future," by Mr. A. L. Bacharach; November 17th, *Liversidge Lecture*, " Reactions of Radicals in Gaseous Systems," by Dr. E. W. R. Steacie; Fellows were invited to all meetings of the Royal Institute of Chemistry, Leeds Area Section, as well as to those organised by other bodies.

*Liverpool.* Joint meetings with the University Chemical Society, the Royal Institute of Chemistry, the Society of Chemical Industry, and the British Association of Chemists. at the University: January 27th, *Lecture*, " Structure and Properties of Synthetic Polypeptides," by Dr. C. H. Bamford; March 3rd, *Lecture*, " The Mode of Action of Pyridoxine," by Dr. H. M. Sinclair; October 13th, *Lecture*, " The Mechanism of the Liquid-phase Oxidation of Decane," by Dr. G. H. Twigg; November 10th, *Lecture*, " The Chromatography of Gases and Vapours," by Dr. F. H. Pollard.

*Manchester.* At the University, unless otherwise stated: January 13th, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, *Lecture*, " Colouring Matters of the Aphididæ," by Sir Alexander Todd; February 17th, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, *Lecture*, " Immunochemistry," by Professor M. Stacey; March 10th, at the College of Technology, *Meeting* for the reading of original papers; April 21st, joint meeting with the Royal Institute of Chemistry, the Society of Chemical Industry, and the Institute of Petroleum, *Symposium*, " Organometallic Compounds," (contributions from the following were read and discussed: Dr. E. A. Braude, Dr. J. Chatt, Professor G. E. Coates, Dr. F. G. Mann, Professor K. Ziegler, and Dr. M. C. Whiting); May 26th, *Centenary Lecture*, " Chemical Effects of Steric Strains," by Professor H. C. Brown; October 5th, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, *Lecture*, " Inorganic Metallurgical Aspects of Atomic Energy," by Mr. L. Rotheram; November 1st, *Centenary Lecture*, " The Photosynthetic Carbon Cycle," by Professor M. Calvin; November 17th, *Meeting* for the reading of original papers; December 1st, joint meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, *Lecture*, " Recent Developments in Fungal Biochemistry," by Dr. J. H. Birkinshaw.

*Newcastle and Durham.* February 11th, at King's College, Newcastle upon Tyne, *Bedson Club Lecture*, " The Place of Theoretical Chemistry in Chemical Education," by Mr. R. P. Bell; February 14th, joint meeting with Durham Colleges Chemical Society, at the University, Durham, *Lecture*, " Some Naturally Occurring Polyacetylenes," by Professor B. Lythgoe; February 25th, at King's College, Newcastle upon Tyne, *Meeting* for the reading

of original papers; March 11th, at King's College, Newcastle upon Tyne, *Bedson Club Lecture*, "The Rapid Reaction of Hæmoglobin with Oxygen and Carbon Monoxide," by Professor F. J. W. Roughton; March 14th, joint meeting with Durham Colleges Chemical Society, at the University, Durham, *Lecture*, "New Developments in Analytical Chemistry," by Dr. R. Belcher; May 13th, at King's College, Newcastle upon Tyne, *Centenary Lecture*, "Chemical Effects of Steric Strains," by Professor H. C. Brown; October 17th, joint meeting with Durham Colleges Chemical Society, at the University, Durham, *Lecture*, "New Aspects of Aromatic Character," by Professor W. Baker; October 26th, at King's College, Newcastle upon Tyne, *Bedson Club Lecture*, "The Photosynthetic Carbon Cycle," by Professor M. Calvin; October 31st, joint meeting with the Durham Colleges Chemical Society, at the University, Durham, *Lecture*, "Recent Researches on the Metal Alkoxides," by Professor W. Wardlaw; November 4th, at King's College, Newcastle upon Tyne, *Meeting* for the reading of original papers; November 25th, at King's College, Newcastle upon Tyne, *Bedson Club Lecture*, "The Relation between Theory and Experiment in Physical Chemistry," by Professor E. A. Guggenheim; November 28th, joint meeting with the Durham Colleges Chemical Society, at the University, Durham, *Lecture*, "Some New Results Obtained by the Method of Flash Photolysis," by Professor R. G. W. Norrish.

*Northern Ireland.* Joint meetings with the Royal Institute of Chemistry and the Society of Chemical Industry at Queen's University, Belfast: January 25th, *Lecture*, "Modern Insecticides and their Uses," by Mr. Q. L. Abel; February 10th, *Tilden Lecture*, "The Rôle of the π-Electron in Aromatic Chemistry," by Professor H. C. Longuet-Higgins; February 22nd, *Lecture*, "The Immunochemistry of the *Pneumococcus* Polysaccharides," by Professor M. Stacey; March 10th, *Lecture*, "The Influence of Structure on Some Properties of Polymers," by Dr. R. J. W. Reynolds; April 26th, *Meeting* for the reading of original papers; September 6th, *Lecture*, "Changing Bread. Some Biochemical and Nutritional Considerations," by Dr. M. Pyke; October 20th, *Lecture*, "Silicones, Their Chemistry and Technology," by Dr. G. G. Freeman; November 22nd, *Lecture*, "Preparation and Use of Radioisotopes in Industry and Medicine," by Dr. G. B. Cook; December 5th, *Lecture*, "Recent Advances in the Vitamin D Field," by Professor B. Lythgoe.

*North Wales.* Joint meetings with the University College of North Wales Chemical Society, at the University College of North Wales, Bangor, unless otherwise stated: January 27th, *Lecture*, "Factors Involved in the Formation of Carbonium Ions," by Professor A. G. Evans; February 17th, joint meeting with the University College of Wales Chemical Society, at the Edward Davies Chemical Laboratories, Aberystwyth, *Lecture*, "Some Aspects of Polysaccharide Research," by Professor S. Peat; February 24th, *Pedler Lecture*, "Some Problems in the Chemistry of the Hemicelluloses," by Professor E. L. Hirst; November 10th, *Lecture*, "Some Experiences in an Industrial Research Laboratory," by Dr. M. A. T. Rogers.

*Nottingham.* Joint meetings with the University Chemical Society, at the University, unless otherwise stated: January 27th, *Lecture*, "Phenylation," by Professor D. H. Hey; February 10th, *Lecture*, "Melting and Crystal Structure," by Professor A. R. Ubbelohde; February 28th, joint meeting with Leicester University College Chemical Society, at University College, Leicester, *Lecture*, "The Kinetics of Halogenation Reactions," by Mr. R. P. Bell; October 17th, joint meeting with Leicester University College Chemical Society, at University College, Leicester, *Lecture*, "Hydrogen-transfer Reactions," by Professor E. A. Braude; November 3rd, joint meeting with Leicester University College Chemical Society, at University College, Leicester, *Lecture*, "Recent Advances in the Chemistry of the Adrenocortical Hormones," by Professor C. W. Shoppee; November 10th, *Lecture*, "New Aspects of Aromatic Character," by Professor Wilson Baker; December 1st, *Lecture*, "Recent Advances in the Physical Chemistry of Sulphur," by Professor G. Gee.

*Oxford.* Joint meetings with the Oxford University Alembic Club, at the Physical Chemistry Laboratory, South Parks Road: June 6th, *Official Meeting and Lecture*, "Some Analytical and Synthetical Studies of Natural Products," by Sir Robert Robinson; October 24th, *Lecture*, "The Structure of Vitamin $B_{12}$," by Mrs. D. M. Hodgkin; November 7th, *Lecture*, "Fluorocarbons—The Basis of a New Chemistry," by Dr. R. N. Haszeldine; November 28th, *Lecture*, "Why Polymerisation Occurs," by Professor F. S. Dainton.

*St. Andrews and Dundee.* January 28th, joint meeting with the University Chemical Society and the Royal Institute of Chemistry, at the University, St. Andrews, *Lecture*, " Recent Advances in Acetylene Chemistry," by Professor R. A. Raphael; February 11th, joint meeting with the University Chemical Society, at the University, St. Andrews, *Lecture*, " The Organic Chemistry of Phosphorus," by Professor H. N. Rydon; February 25th, joint meeting with the University Chemical Society, at the University, St. Andrews, *Lecture*, " Radiation Chemistry," by Professor F. S. Dainton; April 15th, joint meeting with the University Chemical Society, at the University, St. Andrews, *Lecture*, " Polymerisation of Vinyl Ethers," by Professor D. D. Eley; November 18th, joint meeting with the University Chemical Society, at St. Salvators College, St. Andrews, *Lecture*, " The Hydrogen-isotope Effect in Reaction Kinetics," by Mr. R. P. Bell; December 8th, at Queen's College, Dundee, *Lecture*, " Magnetism and the Structure of Inorganic Molecules," by Professor R. S. Nyholm.

*Sheffield.* At the University: January 27th, joint meeting with Sheffield University Chemical Society, *Lecture*, " Some Naturally Occurring Polyacetylenes," by Professor B. Lythgoe; March 3rd, joint meeting with Sheffield University Chemical Society, *Lecture*, " Structures and Properties of Clathrate Compounds," by Mr. H. M. Powell; May 23rd, joint meeting with Sheffield University Chemical Society, *Centenary Lecture*, " Some Chemical Effects of Steric Strains," by Professor H. C. Brown; October 27th, joint meeting with Sheffield University Chemical Society, *Lecture*, " Chemical Effects of Intramolecular Strains," by Dr. G. Baddeley; November 10th, joint meeting with the Royal Institute of Chemistry and Sheffield University Chemical Society, *Lecture*, " Melting and Crystal Structure," by Professor A. R. Ubbelohde; December 1st, joint meeting with Sheffield University Chemical Society, *Lecture*, " Directing Effects in Inorganic Substitution Reactions," by Dr. J. Chatt.

*Southampton.* At the University unless otherwise stated: January 14th, joint meeting with Portsmouth and District Chemical Society, at the College of Technology, Portsmouth, *Lecture*, " Fission Products," by Mr. P. E. Carter; February 4th, joint meeting with Southampton University Chemical Society, *Lecture*, " Recent Investigations in the Field of Vinyl Polymerisation," by Dr. C. H. Bamford; February 18th, joint meeting with Southampton University Chemical Society and the Royal Institute of Chemistry, *Lecture*, " Recent Work on Inclusion Compounds," by Professor Wilson Baker; February 25th, joint meeting with Southampton University Chemical Society, *Lecture*, " Mineral Analysis," by Professor L. S. Theobald; March 11th, joint meeting with Southampton University Chemical Society, *Lecture*, " Reactions in Liquid Dinitrogen Tetroxide," by Dr. C. C. Addison; May 6th, joint meeting with Southampton University Chemical Society, *Lecture*, " Kinetics of Some Organic Reactions," by Mr. R. P. Bell; October 14th, joint meeting with Southampton University Chemical Society and the Royal Institute of Chemistry, *Lecture*, " Recent Developments in Acetylene and Allene Chemistry," by Professor E. R. H. Jones; November 25th, joint meeting with Southampton University Chemical Society, *Lecture*, " Melting and Crystal Structure," by Professor A. R. Ubbelohde; December 1st, joint meeting with the Plastics Institute and the University of Southampton Chemical Society, *Lecture*, " Principles and Practice of Polymer Design," by Mr. R. B. Richards.

*South Wales.* January 24th, at University College, Cardiff, *Lecture*, " Some Recent Advances in Photochemistry," by Professor R. G. W. Norrish; February 4th, joint meeting with University College of Swansea Chemical Society, at University College, Swansea, *Lecture*, " The Adsorption of Vapours by Solids," by Professor D. H. Everett; February 7th, at University College, Cardiff, *Tilden Lecture*, " Molecular Rearrangements," by Professor M. J. S. Dewar; March 11th, joint meeting with the Royal Institute of Chemistry and the University College of Swansea Chemical Society, at University College, Swansea, *Lecture*, " Chemistry of Colchicine," by Dr. J. W. Cook; October 24th, at University College, Cardiff, *Lecture*, " Trapped Radicals in Polymerisation Reactions," by Dr. C. H. Bamford; November 4th, at University College, Swansea, *Lecture*, " The Physical Chemistry of Sulphur," by Professor G. Gee.

## APPENDIX B.

### ANNUAL REPORT OF THE JOINT LIBRARY COMMITTEE FOR THE YEAR 1955.

The past year has witnessed some very considerable changes in the Library.

Early in June new premises became available in Savile Row suitable for conversion into a bookstore and publications stockroom, and during the summer closure some 10,000 volumes were transferred from Burlington House to this new store. The stock of the Society's publications was also transferred to this new store and in turn released space for another bookstore in Burlington House. Further space was obtained by the sale of some 2,000 volumes of periodicals deemed to contain little of interest to chemists. The stock of books throughout the building was then adjusted to make room for the expansion of periodicals and to make the library annexe available to readers. The overall effect is to provide additional storage for a few years.

While this movement of books was in progress the Library was completely redecorated and refurnished in an appropriate style with changes in lay-out to provide better display of periodicals, more table space per reader, a clearer floor area, and better working facilities for the staff. The work necessitated the movement of almost every one of the 60,000 volumes in the Library.

The transference of administrative staff to Savile Row released an office for the Librarian and his typist and also a room which has been converted to house the photo-copying equipment.

The Library regulations have been reviewed and amended where necessary to bring them into line with modern practice and to improve the general administration of the Library.

The facilities offered by the Science Library and National Central Library are now available to readers, and much use has already been made of them.

*Analysis.*

| | Attendances. | Books borrowed. | Additions. Books | Pamphlets |
|---|---|---|---|---|
| 1955* | 7457 | 5854 (2630 by post) | 209 | 35 |
| 1954 | 9370 | 7706 (3000 by post) | 410 | 69 |

* In 1955 the Library was closed for six weeks. The numbers of volumes added in 1955 and 1954 are not strictly comparable as there is some doubt as to whether the methods by which the statistics were compiled were the same in the two years.

Gifts have been made to the Library during the year, and the Committee tenders its grateful thanks to those Fellows and Publishers who have helped the Library in this way.

INCOME AND EXPENDITURE ACCOUNTS

| 1954 | *Expenditure.* | | 1955 |
|---|---|---|---|
| | **GENERAL PURPOSES.** | £ | £ |
| | Administration Expenses: | | |
| | Salaries, Superannuation, etc. ... ... ... ... ... | 5,267 | |
| | House Expenses, etc. ... ... ... ... ... ... ... | 518 | |
| | Stationery, Postages and Office Expenses ... ... ... | 974 | |
| | Miscellaneous ... ... ... ... ... ... ... ... ... | 265 | |
| | | | 7,024 |
| | Meetings ... ... ... ... ... ... ... ... ... ... | | 1,567 |
| | Local Representatives Expenses ... ... ... ... ... | | 1,068 |
| | Travelling Expenses ... ... ... ... ... ... ... ... | | 478 |
| | Capital improvements, Burlington House and Savile Row | 11,811 | |
| | *Less* Grant from Chemical Council ... ... ... ... | 10,000 | |
| | | 1,811 | |
| | *Less* Transfer to Publications Account... ... ... ... | 1,356 | |
| | | | 455 |
| | Transfers: | | |
| | Publications Account— | | |
| | Cost of free publications to Fellows under 27 years of age ... ... ... ... ... ... ... ... ... ... | 1,691 | |
| | Library Account: | | |
| | Capital Expenditure ... ... ... ... ... ... ... | 2,601 | |
| | Maintenance ... ... ... ... ... ... ... ... ... | 1,133 | |
| | Staff Pensions Fund ... ... ... ... ... ... ... | 800 | |
| | General Reserve ... ... ... ... ... ... ... ... | 5,000 | |
| | | | 11,225 |
| | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... ... ... ... ... ... ... | | 246 |
| | | | £22,063 |

**STAFF PENSIONS FUND.**

| £ | | £ |
|---|---|---|
| 855 | Pensions ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 942 |
| 6 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... | 9 |
| 83 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet ... ... ... ... ... ... ... ... ... ... ... ... | 76 |
| £944 | | £1027 |

SOCIETY.

FOR THE YEAR ENDED 31ST DECEMBER, 1955.

| 1954 | *Income.* | | 1955 |
|---|---|---|---|
| | | £ | £ |
| | Fellows' Subscriptions : | | |
| | For 1955 ... ... ... ... ... ... ... ... ... ... | 17,019 | |
| | For 1954 and previous years ... ... ... ... ... ... | 488 | |
| | | 17,507 | |
| | *Add* Income Tax recoverable on Subscriptions under Covenant ... ... ... ... ... ... ... ... ... ... | 1,063 | |
| | | | 18,570 |
| | Income from Investments ... ... ... ... ... ... ... | | 2,549 |
| | Miscellaneous ... ... ... ... ... ... ... ... ... | | 944 |
| | | | £22,063 |

| £ | | £ |
|---|---|---|
| 826 | Transfer from General Purposes Account and Refund of Premiums | 834 |
| 99 | Income from Investments ... ... ... ... ... ... ... ... ... ... | 188 |
| 19 | Deposit Interest ... ... ... ... ... ... ... ... ... ... ... | 5 |
| £944 | | £1027 |

INCOME AND EXPENDITURE ACCOUNTS

| 1954 | *Expenditure.* | | 1955 |
|---|---|---|---|
| | **PUBLICATIONS.** | | |
| | | £ | £ |
| | Journal of the Chemical Society : | | |
| | Salaries and General Expenses ... ... ... ... ... | 8,933 | |
| | Printing and Paper... ... ... ... ... ... ... ... | 33,683 | |
| | Distribution ... ... ... ... ... ... ... ... ... | 3,608 | |
| | | | 46,224 |
| | Annual Reports on the Progress of Chemistry ... ... | | 3,602 |
| | Quarterly Reviews ... ... ... ... ... ... ... ... | | 3,546 |
| | Current Chemical Papers ... ... ... ... ... ... ... | | 4,320 |
| | Transfer from General Purposes Account : | | |
| | Capital improvements, Burlington House and Savile Row ... ... ... ... ... ... ... ... ... ... | | 1,356 |
| | Balance, being Excess of Income over Expenditure, carried to Balance Sheet ... ... ... ... ... ... | | 1,220 |
| | | | £60,268 |

**SPECIAL PUBLICATIONS FUND.**

| | | | |
|---|---|---|---|
| £ | | | £ |
| 333 | Cost of Publications ... ... ... ... ... ... ... ... ... ... ... | | 694 |
| 21 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... | | 36 |
| 381 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet ... ... ... ... ... ... ... ... ... ... ... | | 68 |
| £735 | | | £798 |

**LIBRARY.**

| | | | | |
|---|---|---|---|---|
| £ | £ | | £ | £ |
| | | Capital Expenditure : | | |
| 1,743 | | Books and Periodicals ... ... ... ... ... ... ... | 2,112 | |
| 1,045 | | Binding ... ... ... ... ... ... ... ... ... ... ... | 427 | |
| 39 | | Furniture ... ... ... ... ... ... ... ... ... ... ... | 62 | |
| | 2,827 | | | 2,601 |
| | | Maintenance : | | |
| 4,459 | | Salaries, Superannuation, etc. ... ... ... ... ... | 5,283 | |
| 614 | | Re-binding ... ... ... ... ... ... ... ... ... | 214 | |
| 315 | | House Expenses, etc. ... ... ... ... ... ... ... | 774 | |
| 245 | | Stationery, Postages and Office Expenses ... ... ... | 428 | |
| 95 | | Miscellaneous ... ... ... ... ... ... ... ... ... | 90 | |
| | 5,728 | | | 6,789 |
| £8,555 | | | | £9,390 |

FOR THE YEAR ENDED 31ST DECEMBER, 1955.

| 1954 | | *Income.* | | 1955 | |
|---|---|---|---|---|---|
| | | | £ | £ | |
| | | Sales and Revenue from Advertisements : | | | |
| | | Journal of the Chemical Society ... ... ... ... ... | 37,516 | | |
| | | Annual Reports on the Progress of Chemistry ... ... | 6,065 | | |
| | | Quarterly Reviews ... ... ... ... ... ... ... ... | 4,886 | | |
| | | Current Chemical Papers ... ... ... ... ... ... | 3,958 | | |
| | | Miscellaneous ... ... ... ... ... ... ... ... ... | 284 | | |
| | | | | 52,709 | |
| | | Income from Investments ... ... ... ... ... ... ... | | 368 | |
| | | Transfer from General Purposes Account : | | | |
| | | Cost of free publications to Fellows under 27 years of age ... ... ... ... ... ... ... ... ... ... ... | | 1,691 | |
| | | Grant : The Chemical Council ... ... ... ... ... ... | | 5,500 | |
| | | | | £60,268 | |
| £ | £ | | | £ | £ |
| 577 | | Sales of Publications and Royalties received ... ... ... ... ... | | 601 | |
| 77 | | Income from Investments ... ... ... ... ... ... ... ... ... ... | | 146 | |
| 81 | | Deposit Interest ... ... ... ... ... ... ... ... ... ... ... | | 51 | |
| | £735 | | | | £798 |
| £ | £ | | £ | £ | |
| | 2,827 | Contribution for Capital Expenditure : Transfer from General Purposes Account ... ... ... | | 2,601 | |
| | | Contributions towards maintenance through the Chemical Council : | | | |
| 1,011 | | Chemical Society ... ... ... ... ... ... ... ... | 1,133 | | |
| 2,292 | | Royal Institute of Chemistry... ... ... ... ... ... | 2,568 | | |
| 752 | | Society of Chemical Industry ... ... ... ... ... | 843 | | |
| 275 | | Faraday Society ... ... ... ... ... ... ... ... | 308 | | |
| 143 | | Society for Analytical Chemistry ... ... ... ... ... | 160 | | |
| 273 | | Biochemical Society ... ... ... ... ... ... | 306 | | |
| 822 | | Chemical Council (Direct Grant) ... ... ... ... ... | 1,311 | | |
| 5,568 | | | 6,629 | | |
| | | Contributions from other sources : | | | |
| 100 | | Association of British Chemical Manufacturers ... ... | 100 | | |
| 50 | | Institute of Brewing ... ... ... ... ... ... ... | 50 | | |
| 10 | | Society of Dyers and Colourists ... ... ... ... ... | 10 | | |
| | 5,728 | | | 6,789 | |
| | £8,555 | | | | £9,390 |

GENERAL BALANCE SHEET—

| *Liabilities.* | | 1955 | |
|---|---|---|---|
| | £ | £ | £ |
| Sundry Creditors ... ... ... ... ... ... ... | | | 13,836 |
| Receipts in Advance : | | | |
| Fellows' Subscriptions ... ... ... ... ... | | 8,693 | |
| Publications Sales ... ... ... ... ... ... | | 18,111 | |
| | | | 26,804 |
| General Reserve ... ... ... ... ... ... ... | | 24,339 | |
| *Add* Transfer from General Purposes Income and Expenditure Account ... ... ... ... ... ... ... | | 5,000 | |
| | | | 29,339 |
| Life Composition Fees— | | | |
| Balance at 1st January, 1955 ... ... ... | | 5,514 | |
| *Add* Receipts during 1955 ... ... ... ... | | 325 | |
| | | | 5,839 |
| Special Funds : | | | |
| Publications ... ... ... ... ... ... ... ... | | 10,979 | |
| Special Publications— | | | |
| Balance at 1st January, 1955 ... ... ... | 6,570 | | |
| *Add* Excess of Income over Expenditure for the year ... ... ... ... ... ... ... ... | 68 | | |
| | | 6,638 | |
| Staff Pensions— | | | |
| Balance at 1st January, 1955 ... ... ... | 5,407 | | |
| *Add* Profit on Change of Investments ... | 8 | | |
| Excess of Income over Expenditure for the year ... ... ... ... ... | 76 | | |
| | | 5,491 | |
| | | | 23,108 |
| Accumulated Fund : | | | |
| Balance at 1st January, 1955 ... ... ... | | 30,262 | |
| *Add* Sale of Surplus Library Books ... ... | | 4,185 | |
| Bureau of Abstracts— | | | |
| Provision not required ... ... ... | 2,000 | | |
| Refund on Liquidation ... ... ... | 582 | | |
| | | 2,582 | |
| Excess of Income over Expenditure for the year— | | | |
| General Purposes ... ... ... ... | 246 | | |
| Publications ... ... ... ... ... ... | 1,220 | | |
| | | 1,466 | |
| | | | 38,495 |
| | | | £137,421 |

We have examined the General Balance Sheet, the Trust and Lecture Fund Balance Sheet Society, and certify them to be in accordance therewith and, in our opinion, correct. We have

FINSBURY CIRCUS HOUSE,
BLOMFIELD STREET, E.C.2
15th MARCH, 1956.

31ST DECEMBER, 1955.

| *Assets.* | £ | 1955 £ | £ |
|---|---|---|---|
| Investments as per Schedule at cost or value when acquired : | | | |
| General Reserve ... ... ... ... ... ... | | 17,822 | |
| Special Funds— | | | |
| Publications ... ... ... ... ... ... ... | 10,979 | | |
| Special Publications ... ... ... ... ... | 4,011 | | |
| Staff Pensions ... ... ... ... ... ... | 5,176 | | |
| | | 20,166 | |
| General Purposes ... ... ... ... ... ... | | 43,487 | |
| | | | 81,475 |
| Sundry Debtors ... ... ... ... ... ... ... | | | 8,078 |
| Stock of Paper and Wrappers ... ... ... ... | | | 6,745 |
| Treasury Bills at cost ... ... ... ... ... ... | | | 24,752 |
| Balances at Bank (including Deposit) and Cash in hand ... ... ... ... ... ... ... ... | | | 16,371 |
| | | | £137,421 |

MICHAEL W. PERRIN, *Honorary Treasurer.*

and accompanying Income and Expenditure Accounts with the Books and Vouchers of the also verified the Balances at the Bankers and Investments.

W. B. KEEN & CO.
*Chartered Accountants.*



LECTURE FUNDS

## TRUST AND

### Income and Expenditure Accounts

| 1954 | *Expenditure.* | 1955 |
|---|---|---|
| | **CENTENARY FUND.** | |
| £ | | £ |
| 549 | Expenses of Lecturers & Delegates ... ... ... ... ... ... ... ... ... ... | 1,270 |
| 44 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 46 |
| 286 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | — |
| £879 | | £1,316 |
| | **CORDAY–MORGAN MEDAL AND PRIZE FUND.** | |
| £ | | £ |
| 158 | Prize ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 210 |
| 6 | Medal ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 10 |
| 30 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 27 |
| 113 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | 62 |
| £307 | | £309 |
| | **CORDAY–MORGAN MEMORIAL FUND.** | |
| £ | | £ |
| 400 | Grant to the Corday–Morgan Memorial Fund Executive ... ... ... ... ... | 400 |
| 6 | Memorial Expenses (Clause 12 of the Will) ... ... ... ... ... ... ... ... | 9 |
| 26 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 27 |
| 94 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | 113 |
| £526 | | £549 |
| | **FARADAY LECTURE FUND.** | |
| £ | | £ |
| 1 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 1 |
| 14 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | 16 |
| £15 | | £17 |
| | **ROBERT JOHN FLINTOFF TRUST.** | |
| £ | | £ |
| 75 | Honorarium ... ... ... ... ... ... ... ... ... ... ... ... ... ... | — |
| 3 | Medal ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... | — |
| 2 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 2 |
| — | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | 33 |
| £80 | | £35 |
| | **EDWARD FRANK HARRISON MEMORIAL TRUST.** | |
| £ | | £ |
| 105 | Prize ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... | — |
| 18 | Plaque ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... ... | — |
| 2 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 2 |
| — | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | 45 |
| £125 | | £47 |

## LECTURE FUNDS.

FOR THE YEAR ENDED 31ST DECEMBER, 1955.

| 1954 | *Income.* | 1955 |
|---|---|---|
| £ | | £ |
| 879 | Income from Investments ... ... ... ... ... ... ... ... ... ... ... ... ... | 932 |
| — | Balance, being Excess of Expenditure over Income, carried to Balance Sheet... | 384 |
| £879 | | £1316 |
| £ | | £ |
| 306 | Income from Investments ... ... ... ... ... ... ... ... ... ... ... ... ... | 309 |
| 1 | Deposit Interest ... ... ... ... ... ... ... ... ... ... ... ... ... ... | — |
| £307 | | £309 |
| £ | | £ |
| 526 | Income from Investments ... ... ... ... ... ... ... ... ... ... ... ... ... | 549 |
| £526 | | £549 |
| £ | | £ |
| 15 | Income from Investment ... ... ... ... ... ... ... ... ... ... ... ... ... | 17 |
| £15 | | £17 |
| £ | | £ |
| 35 | Income from Investments ... ... ... ... ... ... ... ... ... ... ... ... ... | 35 |
| 45 | Balance, being Excess of Expenditure over Income, carried to Balance Sheet... | — |
| £80 | | £35 |
| £ | | £ |
| 47 | Income from Investments... ... ... ... ... ... ... ... ... ... ... ... ... | 47 |
| 78 | Balance, being Excess of Expenditure over Income, carried to Balance Sheet... | — |
| £125 | | £47 |

| 1954 | *Expenditure.* | 1955 |
|---|---|---|
| | **RESEARCH FUND.** | |
| £ | | £ |
| 744 | Grants awarded ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 668 |
| 21 | Honorarium, Hugo Müller Lecture ... ... ... ... ... ... ... ... ... ... | — |
| — | Honorarium, Longstaff Medallist ... ... ... ... ... ... ... ... ... ... | 20 |
| 94 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 67 |
| — | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | 120 |
| £859 | | £875 |
| | **SPECIAL LECTURES FUND.** | |
| £ | | £ |
| 26 | Honoraria ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 52 |
| 3 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 3 |
| 21 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | — |
| £50 | | £55 |
| | **TILDEN LECTURE FUND.** | |
| £ | | £ |
| 16 | Honoraria ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 31 |
| 21 | Lecture Expenses ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 18 |
| 3 | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 4 |
| 32 | Balance, being Excess of Income over Expenditure, carried to Balance Sheet... | 24 |
| £72 | | £77 |

FOR THE YEAR ENDED 31ST DECEMBER, 1955.

| 1954 | *Income.* | 1955 |
|---|---|---|
| £ | | £ |
| 750 | Income from Investments ... ... ... ... ... ... ... ... ... ... ... ... ... | 750 |
| 3 | Deposit Interest ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 7 |
| 63 | Grants repaid or not claimed ... ... ... ... ... ... ... ... ... ... ... ... | 107 |
| — | Miscellaneous ... ... ... ... ... ... ... ... ... ... ... ... ... ... | 11 |
| 43 | Balance, being Excess of Expenditure over Income, carried to Balance Sheet... | — |
| £859 | | £875 |

| | | |
|---|---|---|
| £ | | £ |
| 50 | Income from Investment ... ... ... ... ... ... ... ... ... ... ... ... ... | 50 |
| — | Balance, being Excess of Expenditure over Income, carried to Balance Sheet... | 5 |
| £50 | | £55 |

| | | |
|---|---|---|
| £ | | £ |
| 71 | Income from Investments... ... ... ... ... ... ... ... ... ... ... ... ... | 77 |
| 1 | Deposit Interest ... ... ... ... ... ... ... ... ... ... ... ... ... ... | — |
| £72 | | £77 |

## TRUST AND

### BALANCE SHEET—

| 1954 | | *Liabilities.* | | 1955 | |
|---|---|---|---|---|---|
| £ | £ | | £ | £ | £ |
| | 1,382 | Sundry Creditors ... ... ... ... ... ... ... | | | 1,003 |
| | | Centenary Fund : | | | |
| | | Capital Account— | | | |
| 28,076 | | Balance at 1st January, 1955 ... ... ... | 29,106 | | |
| 1,030 | | *Add* Contributions for the year ... ... ... | 1,026 | | |
| | 29,106 | | | 30,132 | |
| | | Income Account— | | | |
| 117 | | Balance at 1st January, 1955 ... ... ... | 403 | | |
| | | *Deduct* Excess of Expenditure over Income | | | |
| — | | for the year ... ... ... ... ... ... | 384 | | |
| | | *Add* Excess of Income over Expenditure | | | |
| 286 | | for the year ... ... ... ... ... ... | — | | |
| | 403 | | | 19 | |
| | | | | | 30,151 |
| | | Corday–Morgan Medal and Prize Fund : | | | |
| | | Capital Account— | | | |
| 5,885 | | Balance at 1st January, 1955 ... ... ... | 5,898 | | |
| — | | *Add* From Public Trustee ... ... ... ... | 44 | | |
| 13 | | Balance of Bonus Issue of Stock ... ... | 1 | | |
| | 5,898 | | | 5,943 | |
| | | Income Account— | | | |
| 1,599 | | Balance at 1st January, 1955 ... ... ... | 1,712 | | |
| | | *Add* Excess of Income over Expenditure | | | |
| 113 | | for the year ... ... ... ... ... ... | 62 | | |
| | 1,712 | | | 1,774 | |
| | | | | | 7,717 |
| | | Corday–Morgan Memorial Fund : | | | |
| | | Capital Account— | | | |
| 10,092 | | Balance at 1st January, 1955 ... ... ... | 10,104 | | |
| 12 | | *Add* Profit on Change of Investments ... | 7 | | |
| — | | From Public Trustee ... ... ... ... | 77 | | |
| | 10,104 | | | 10,188 | |
| | | Income Account— | | | |
| 2,778 | | Balance at 1st January, 1955 ... ... ... | 2,872 | | |
| | | *Add* Excess of Income over Expenditure | | | |
| 94 | | for the year ... ... ... ... ... ... | 113 | | |
| | 2,872 | | | 2,985 | |
| | | | | | 13,173 |
| | | Faraday Lecture Fund : | | | |
| 487 | | Balance at 1st January, 1955 ... ... ... ... ... | | 501 | |
| 14 | | *Add* Excess of Income over Expenditure for the year... | | 16 | |
| | 501 | | | | 517 |
| | | Robert John Flintoff Trust : | | | |
| 1,111 | | Balance at 1st January, 1955 ... ... ... ... ... | | 1,066 | |
| — | | *Add* Excess of Income over Expenditure for the year... | | 33 | |
| 45 | | *Deduct* Excess of Expenditure over Income for the year | | — | |
| | 1,066 | | | | 1,099 |
| | | Edward Frank Harrison Memorial Trust : | | | |
| 1,204 | | Balance at 1st January, 1955 ... ... ... ... ... | | 1,126 | |
| — | | *Add* Excess of Income over Expenditure for the year... | | 45 | |
| 78 | | *Deduct* Excess of Expenditure over Income for the year | | — | |
| | 1,126 | | | | 1,171 |
| | | Research Fund : | | | |
| 23,982 | | Balance at 1st January, 1955 ... ... ... ... ... | | 23,939 | |
| — | | *Add* Excess of Income over Expenditure for the year... | | 120 | |
| 43 | | *Deduct* Excess of Expenditure over Income for the year | | — | |
| | 23,939 | | | | 24,059 |
| | | Special Lectures Fund : | | | |
| 1,724 | | Balance at 1st January, 1955 ... ... ... ... ... | | 1,745 | |
| — | | *Deduct* Excess of Expenditure over Income for the year | | 5 | |
| 21 | | *Add* Excess of Income over Expenditure for the year... | | — | |
| | 1,745 | | | | 1,740 |
| | | Tilden Lecture Fund : | | | |
| 2,060 | | Balance at 1st January, 1955 ... ... ... ... ... | | 2,092 | |
| 32 | | *Add* Excess of Income over Expenditure for the year... | | 24 | |
| | 2,092 | | | | 2,116 |
| | £81,946 | | | | £82,746 |

## LECTURE FUNDS.

**31ST DECEMBER, 1955.**

| 1954 | | *Assets.* | 1955 | |
|---|---|---|---|---|
| £ | £ | | £ | £ |
| | 1,550 | Sundry Debtors ... ... ... ... ... ... ... ... ... | | 1,288 |
| | | Investments as per Schedule at cost or value when acquired : | | |
| 27,698 | | Centenary Fund ... ... ... ... ... ... ... ... | 29,198 | |
| 7,371 | | Corday–Morgan Medal and Prize Fund ... ... ... | 7,371 | |
| 12,239 | | Corday–Morgan Memorial Fund ... ... ... ... ... | 12,239 | |
| 469 | | Faraday Lecture Fund ... ... ... ... ... ... ... | 469 | |
| 1,000 | | Robert John Flintoff Trust ... ... ... ... ... ... | 1,000 | |
| 1,102 | | Edward Frank Harrison Memorial Trust ... ... ... | 1,101 | |
| 23,923 | | Research Fund ... ... ... ... ... ... ... ... ... | 23,923 | |
| 1,615 | | Special Lectures Fund ... ... ... ... ... ... ... | 1,615 | |
| 1,979 | | Tilden Lecture Fund ... ... ... ... ... ... ... | 1,979 | |
| | 77,396 | | | 78,895 |
| | 3,000 | Balances at Bank (including Deposit) ... ... ... ... | | 2,563 |
| | £81,946 | | | £82,746 |

SCHEDULE OF INVESTMENTS,

## GENERAL

| *Nominal Details.* | | | | | *Cost or Value when Acquired.* | | |
|---|---|---|---|---|---|---|---|
| | | | | | £ | £ | £ |
| **GENERAL RESERVE.** | | | | | | | |
| £1,500 | 0s. | 0d. | 3% | Savings Bonds, 1955/65 ... ... ... ... | 1,489 | | |
| £1,250 | 0s. | 0d. | 3% | Funding Stock, 1959/69 ... ... ... ... | 1,218 | | |
| £1,165 | 0s. | 0d. | 2½% | Funding Stock, 1956/61 ... ... ... ... | 1,169 | | |
| £1,800 | 0s. | 0d. | 3½% | Defence Bonds (Conversion Issue) ... ... | 1,789 | | |
| £1,000 | 0s. | 0d. | 3% | Sheffield Corporation Stock, 1967/69 ... | 963 | | |
| £2,582 | 10s. | 9d. | 3% | Liverpool Corporation Stock, 1955/58 ... | 2,647 | | |
| £1,500 | 0s. | 0d. | 3% | Ceylon Stock, 1959/64... ... ... ... ... | 1,439 | | |
| £1,000 | 0s. | 0d. | 3½% | Agricultural Mortgage Corporation, Ltd., Deb. Stock, 1961/63 ... ... ... ... | 1,020 | | |
| £1,000 | 0s. | 0d. | 3¼% | Covent Garden Properties, Ltd., Red. Deb. Stock, 1968 ... ... ... ... ... ... | 951 | | |
| £1,000 | 0s. | 0d. | 4% | Cable and Wireless (Holding), Ltd., 10 year Red. Unsec. Stock, 1960 ... ... ... | 1,015 | | |
| £1,100 | 0s. | 0d. | 4½% | Nelson Financial Trust, Ltd., Deb. Stock, 1970 ... ... ... ... ... ... ... ... | 982 | | |
| £1,000 | 0s. | 0d. | 4% | Dominion and General Trust, Ltd., Red. Deb. Stock, 1959/64 ... ... ... ... | 987 | | |
| £1,000 | 0s. | 0d. | 4½% | Rugby Portland Cement Co., Ltd., Unsec. Stock, 1957/62 ... ... ... ... ... | 1,040 | | |
| £1,000 | 0s. | 0d. | 5½% | Clan Line Steamers, Ltd., Cum. Red. 1st "B" Pref. Stock ... ... ... ... ... | 1,113 | | |
| | | | | (Market Value £16,080) | | | 17,822 |
| **SPECIAL FUNDS.** | | | | | | | |
| **PUBLICATIONS.** | | | | | | | |
| £2,260 | 19s. | 9d. | 3½% | Conversion Stock, 1961, or after ... ... | 1,567 | | |
| £1,000 | 0s. | 0d. | 3% | Savings Bonds, 1955/65 ... ... ... ... | 1,000 | | |
| £2,261 | 1s. | 11d. | 3% | Savings Bonds, 1960/70 ... ... ... ... | 2,276 | | |
| £2,175 | 13s. | 4d. | 3% | British Transport Guaranteed Stock, 1978/88 ... ... ... ... ... ... ... | 1,929 | | |
| £2,000 | 0s. | 0d. | 3% | British Electricity Guaranteed Stock, 1968/73 ... ... ... ... ... ... ... | 2,002 | | |
| £1,200 | 0s. | 0d. | 3% | Commonwealth of Australia Registered Stock, 1964/66 ... ... ... ... ... | 1,205 | | |
| £982 | 12s. | 0d. | 3% | Southern Rhodesia Stock, 1971/73 ... ... | 1,000 | | |
| | | | | (Market Value £9,421) | | 10,979 | |
| **SPECIAL PUBLICATIONS.** | | | | | | | |
| £745 | 9s. | 3d. | 3½% | Conversion Stock, 1961, or after ... ... | 569 | | |
| £746 | 1s. | 0d. | 3% | British Transport Guaranteed Stock, 1978/88 ... ... ... ... ... ... ... | 720 | | |
| £755 | 0s. | 0d. | 3% | British Electricity Guaranteed Stock, 1968/73 ... ... ... ... ... ... ... | 751 | | |
| £1,000 | 0s. | 0d. | 3½% | London County Consolidated Stock, 1968/73 ... ... ... ... ... ... ... ... | 997 | | |
| £1,000 | 0s. | 0d. | 4% | Government of the Fed. of Rhodesia and Nyasaland Stock, 1972/74 ... ... ... | 974 | | |
| | | | | (Market Value £3,432) | | 4,011 | |
| **STAFF PENSIONS.** | | | | | | | |
| £119 | 0s. | 1d. | 3½% | Conversion Stock, 1961, or after ... ... | 93 | | |
| £170 | 0s. | 0d. | 3% | Savings Bonds, 1955/65 ... ... ... ... | 170 | | |
| £1,000 | 0s. | 0d. | 3½% | Defence Bonds ... ... ... ... ... ... | 1,000 | | |
| £1,505 | 0s. | 0d. | 3½% | Defence Bonds (Conversion Issue) ... ... | 1,496 | | |
| £1,500 | 0s. | 0d. | 3% | Sheffield Corporation, Red. Deb. Stock, 1967/69 ... ... ... ... ... ... ... | 1,442 | | |
| £1,000 | 0s. | 0d. | 3¼% | Southern Rhodesia Stock, 1955/65 ... ... | 975 | | |
| | | | | (Market Value £4,829) | | 5,176 | |
| | | | | | | | 20,166 |
| | | | | Carried forward | | | £37,988 |

AT 31ST DECEMBER, 1955.

## FUNDS.

| *Nominal Details.* | | | | *Cost or Value when Acquired.* | |
|---|---|---|---|---|---|
| | | | | £ | £ |
| | | | Brought forward | | £37,988 |
| | | | **GENERAL PURPOSES.** | | |
| £2,609 | 14s. 4d. | 3½% | Conversion Stock, 1961, or after ... ... ... ... | 2,045 | |
| £2,000 | 0s. 0d. | 3% | Savings Bonds, 1965/75 ... ... ... ... ... ... | 2,006 | |
| £1,000 | 0s. 0d. | 3% | Funding Stock, 1959/69 ... ... ... ... ... ... | 973 | |
| £200 | 0s. 0d. | 3½% | Defence Bonds (Conversion Issue) ... ... ... ... | 199 | |
| £1,000 | 0s. 0d. | 3½% | Defence Bonds ... ... ... ... ... ... ... ... | 1,000 | |
| £4,747 | 4s. 6d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | 5,705 | |
| £2,546 | 1s. 4d. | 3% | British Electricity Guaranteed Stock, 1968/73 ... | 2,549 | |
| £2,053 | 7s. 5d. | 4% | Consolidated Stock, 1957, or after ... ... ... ... | 1,978 | |
| £2,425 | 8s. 9d. | 3% | Commonwealth of Australia Registered Stock, 1964/66 ... ... ... ... ... ... ... ... ... | 2,435 | |
| £A3,000 | 0s. 0d. | 3⅛% | Commonwealth of Australia Treasury Bonds, 1961/64 ... ... ... ... ... ... ... ... ... | 2,553 | |
| £1,000 | 0s. 0d. | 4% | Canadian Pacific Railway Perp. Deb. Stock ... ... | 838 | |
| £766 | 0s. 0d. | 3½% | London Trust Co., Ltd., Red. Deb. Stock ... ... | 576 | |
| £1,000 | 0s. 0d. | 4% | Rolls-Royce, Ltd., Red. Deb. Stock, 1974/84 ... | 1,007 | |
| £925 | 0s. 0d. | 4% | Olympia, Ltd., 1st Mort. Red. Deb. Stock ... ... | 853 | |
| £1,000 | 0s. 0d. | 5½% | Wankie Colliery Co., Ltd., Mort. Deb. Stock... ... | 1,149 | |
| 800 | | 6% | Rotary Hoes, Ltd., Red. Cum. Pref. £1 Shares ... | 840 | |
| 750 | | 7½% | Scottish and Mercantile Investment Co., Ltd., Cum. Pref. £1 Shares ... ... ... ... ... ... ... | 940 | |
| £500 | 0s. 0d. | 8% | British Petroleum Co., Ltd., Cum. First Pref. Stock | 779 | |
| 1,000 | | 5% | Bell London & Provincial Props. Ltd., Cum. Pref. £1 Shares ... ... ... ... ... ... ... ... | 884 | |
| 900 | | 6½% | J. & N. Phillips & Co., Ltd., Cum. Pref. £1 Shares... | 930 | |
| 1,000 | | 5% | Geo. Sandeman & Sons, Ltd., Cum. Pref. £1 Shares | 938 | |
| £1,000 | 0s. 0d. | 4½% | London Midland Associated Properties, Ltd., Cum. Pref. Stock ... ... ... ... ... ... ... ... | 775 | |
| 160 | | | Allen & Hanburys, Ltd., Ord. £1 Shares ... ... | 521 | |
| £440 | 0s. 0d. | | Cable & Wireless (Holding), Ltd., Ord. Stock ... | 549 | |
| £50 | 0s. 0d. | | Commercial Union Assurance Co., Ltd., Stock ... | 581 | |
| £300 | 0s. 0d. | | Goodlass Wall & Lead Industries, Ltd., Ord. Stock | 497 | |
| £435 | 0s. 0d. | | Leyland Motors, Ltd., Ord. Stock ... ... ... ... | 702 | |
| £180 | 0s. 0d. | | Shell Transport and Trading Co., Ltd., Ord. Stock | 666 | |
| £640 | 0s. 0d. | | Peninsular and Oriental Steam Navigation Co., Ltd., Def. Stock ... ... ... ... ... ... ... ... | 504 | |
| £400 | 0s. 0d. | | Tube Investments, Ltd., Ord. Stock ... ... ... | 926 | |
| 1,500 | | | Home and Colonial Stores, Ltd., Ord. 6s. 8d. Shares | 794 | |
| £396 | 0s. 0d. | | British Insulated Callender's Cables, Ltd., Ord. Stock ... ... ... ... ... ... ... ... | 866 | |
| 500 | | | Trust Houses, Ltd., Ord. £1 Shares... ... ... ... | 700 | |
| £480 | 0s. 0d. | | Charterhouse Investment Trust, Ltd., Ord. Stock... | 847 | |
| 600 | | | Consolidated Zinc Corporation, Ltd., Ord. £1 Shares | 940 | |
| £300 | 0s. 0d. | | Smiths Stamping Works (Coventry), Ltd., Ord. Stock ... ... ... ... ... ... ... ... ... | 889 | |
| £275 | 0s. 0d. | | West of England Sack Contractors, Ltd., Ord. Stock | 768 | |
| 1,000 | | | John Shaw and Sons (Wolverhampton), Ltd., 5s. Shares ... ... ... ... ... ... ... ... ... | 785 | |
| | | | (Market Value £41,682) | | 43,487 |
| | | | | | £81,475 |

SCHEDULE OF INVESTMENTS,

## TRUST AND

| *Nominal Details.* | | | | | *Cost or Value when Acquired.* | |
|---|---|---|---|---|---|---|
| | | | | | £ | £ |
| **CENTENARY FUND.** | | | | | | |
| £2,637 | 10s. | 6d. | 3½% | Conversion Stock, 1961, or after ... ... ... ... | 2,300 | |
| £2,477 | 13s. | 11d. | 3% | Savings Bonds, 1955/65 ... ... ... ... ... ... | 2,492 | |
| £2,500 | 0s. | 0d. | 3% | Savings Bonds, 1960/70 ... ... ... ... ... ... | 2,534 | |
| £2,705 | 18s. | 7d. | 2½% | Savings Bonds, 1964/67 ... ... ... ... ... ... | 2,500 | |
| £2,279 | 13s. | 0d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | 2,237 | |
| £2,500 | 0s. | 0d. | 3% | British Electricity Guaranteed Stock, 1968/73 ... | 2,499 | |
| £4,933 | 15s. | 11d. | 4% | Consolidated Stock, 1957, or after ... ... ... | 4,500 | |
| £2,302 | 19s. | 6d. | 3½% | Agricultural Mortgage Corporation, Ltd., Deb. Stock, 1975/78 ... ... ... ... ... ... ... | 2,000 | |
| £1,540 | 2s. | 7d. | 4¼% | Glasgow Corporation Stock, 1966/68 ... ... ... | 1,500 | |
| £1,970 | 1s. | 0d. | 3% | New Zealand Stock, 1973/77 ... ... ... ... | 2,000 | |
| £1,716 | 15s. | 2d. | 3½% | Northern Ireland Stock, 1969/71 ... ... ... ... | 1,700 | |
| £A3,500 | 0s. | 0d. | 3½% | Commonwealth of Australia Treasury Bonds, 1961/64 ... ... ... ... ... ... ... ... ... ... | 2,936 | |
| | | | | (Market Value £24,971) | | 29,198 |
| **CORDAY-MORGAN MEDAL AND PRIZE FUND.** | | | | | | |
| £1,951 | 8s. | 2d. | 3½% | War Stock, 1952, or after ... ... ... ... ... | 1,826 | |
| £635 | 3s. | 10d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | 575 | |
| £640 | 15s. | 5d. | 4% | Consolidated Stock, 1957, or after ... ... ... | 648 | |
| £774 | 6s. | 3d. | 3% | British Guiana Government Stock, 1975/80 ... | 690 | |
| £137 | 10s. | 0d. | 3% | Federated Malay States Government Stock, 1960/70 ... ... ... ... ... ... ... ... ... ... | 120 | |
| £137 | 10s. | 0d. | 3½% | Bournemouth Corporation Red. Stock, 1958/62 ... | 134 | |
| £300 | 0s. | 0d. | 3½% | Hertfordshire County Red. Stock, 1954/59 ... ... | 298 | |
| £134 | 0s. | 0d. | | Barclays Bank (D. C. & O.), " A " Ord. Stock ... | 201 | |
| £258 | 0s. | 0d. | | Mitchells & Butlers, Ltd., Ord. Stock ... ... ... | 714 | |
| £206 | 0s. | 0d. | | Watney Combe Reid & Co., Ltd., Def. Ord. Stock | 597 | |
| £83 | 0s. | 0d. | | Imperial Tobacco Co. (G.B. & I.) Ltd., Ord. Stock | 263 | |
| £240 | 0s. | 0d. | | Cardinal Investment Trust, Ltd., Def. Stock ... | 291 | |
| £104 | 0s. | 0d. | | Commercial Union Assurance Co., Ltd., Stock ... | 1,014 | |
| | | | | (Market Value £7,603) | | 7,371 |
| **CORDAY-MORGAN MEMORIAL FUND.** | | | | | | |
| £1,530 | 2s. | 5d. | 3½% | Conversion Stock, 1961, or after ... ... ... ... | 1,426 | |
| £1,973 | 16s. | 11d. | 3½% | War Stock, 1952, or after ... ... ... ... ... | 1,880 | |
| £477 | 1s. | 10d. | 3% | British Electricity Guaranteed Stock, 1968/73 ... | 451 | |
| £1,062 | 10s. | 11d. | 3% | British Gas Guaranteed Stock, 1990/95 ... ... | 894 | |
| £413 | 13s. | 7d. | 4% | Consolidated Stock, 1957 ... ... ... ... ... | 413 | |
| £217 | 12s. | 6d. | 3% | London County Consolidated Stock, 1962/67 ... | 208 | |
| £1,035 | 0s. | 7d. | 3% | Redemption Stock, 1986/96 ... ... ... ... ... | 929 | |
| £137 | 10s. | 0d. | 4½% | Kenya Government Stock, 1961/71 ... ... ... | 149 | |
| £300 | 0s. | 0d. | 4¼% | New Zealand Government Stock, 1970/73 ... ... | 299 | |
| £1,000 | 0s. | 0d. | 4% | South Staffordshire Waterworks Red. Pref. Stock, 1971 ... ... ... ... ... ... ... ... ... | 1,047 | |
| £300 | 0s. | 0d. | 3½% | Hull Corporation Red. Stock, 1973/75 ... ... ... | 304 | |
| £108 | 0s. | 0d. | | Barclays Bank, Ltd., " B " Ord. Stock ... ... | 237 | |
| £309 | 0s. | 0d. | | Benskins Watford Brewery, Ltd., Ord. Stock ... | 685 | |
| £206 | 0s. | 0d. | | H. & G. Simmonds, Ltd., Ord. Stock ... ... ... | 824 | |
| £160 | 0s. | 0d. | | Imperial Tobacco Co. (G.B. & I.) Ltd., Ord. Stock | 506 | |
| £108 | 0s. | 0d. | | Thomas Tilling, Ltd., Ord. Stock ... ... ... ... | 107 | |
| £340 | 0s. | 0d. | 4½% | Alliance Trust, Ltd., Deb. Stock, 1956 ... ... | 344 | |
| £69 | 0s. | 0d. | | London & Lancashire Insurance Co., Ltd., Ord. Stock ... ... ... ... ... ... ... ... ... | 448 | |
| 68 | | | | Phœnix Assurance Co., Ltd., Ord. £1 Shares ... | 1,088 | |
| | | | | (Market Value £11,448) | | 12,239 |
| | | | | Carried forward | | £48,808 |

AT 31ST DECEMBER, 1955.

## LECTURE FUNDS.

| *Nominal Details.* | | | | | *Cost or Value when Acquired.* | |
|---|---|---|---|---|---|---|
| | | | | | £ | £ |
| | | | | Brought forward | | 48,808 |
| **FARADAY LECTURE FUND.** | | | | | | |
| £473 | 8s. | 9d. | 3½% | Conversion Stock, 1961, or after ... ... ... ... | | 469 |
| | | | | (Market Value £362) | | |
| **ROBERT JOHN FLINTOFF TRUST.** | | | | | | |
| £523 | 2s. | 2d. | 3½% | Conversion Stock, 1961, or after ... ... ... ... | 500 | |
| £545 | 19s. | 4d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | 500 | |
| | | | | (Market Value £801) | | 1,000 |
| **EDWARD FRANK HARRISON MEMORIAL TRUST.** | | | | | | |
| £61 | 15s. | 8d. | 3½% | Conversion Stock, 1961, or after ... ... ... ... | 50 | |
| £1,489 | 10s. | 6d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | 1,051 | |
| | | | | (Market Value £1,142) | | 1,101 |
| **RESEARCH FUND.** | | | | | | |
| £4,177 | 16s. | 1d. | 3½% | Conversion Stock, 1961, or after ... ... ... ... | 3,626 | |
| £500 | 0s. | 0d. | 3% | Defence Bonds, 4th issue ... ... ... ... ... ... | 500 | |
| £1,835 | 0s. | 0d. | 2½% | Funding Stock, 1956/61 ... ... ... ... ... ... | 1,835 | |
| £1,500 | 0s. | 0d. | 3% | Savings Bonds, 1955/65 ... ... ... ... ... ... | 1,515 | |
| £4,000 | 0s. | 0d. | 3% | Savings Bonds, 1960/70 ... ... ... ... ... ... | 4,060 | |
| £3,755 | 2s. | 1d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | 3,568 | |
| £3,719 | 8s. | 2d. | 3% | British Electricity Guaranteed Stock, 1968/73 ... | 3,724 | |
| £4,000 | 0s. | 0d. | 3% | Commonwealth of Australia Registered Stock, 1964/66 ... ... ... ... ... ... ... ... ... | 4,015 | |
| £1,116 | 7s. | 0d. | 3% | New Zealand Stock, 1973/77 ... ... ... ... ... | 1,080 | |
| | | | | (Market Value £19,872) | | 23,923 |
| **SPECIAL LECTURES FUND.** | | | | | | |
| £1,669 | 17s. | 3d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | | 1,615 |
| | | | | (Market Value £1,227) | | |
| **TILDEN LECTURE FUND.** | | | | | | |
| £419 | 4s. | 10d. | 3% | Funding Stock, 1959/69 ... ... ... ... ... ... | 387 | |
| £792 | 10s. | 8d. | 3% | British Transport Guaranteed Stock, 1978/88 ... | 725 | |
| 186 | | | | National Provincial Bank Ltd. " B " Shares £5 each, £1 paid ... ... ... ... ... ... ... ... ... | 679 | |
| £220 | 0s. | 0d. | 3% | Metropolitan Water Board (Kent Water Works) Deb. Stock ... ... ... ... ... ... ... ... | 188 | |
| | | | | (Market Value £1,715) | | 1,979 |
| | | | | | | £78,895 |

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| **Dicyclopropyl ketone** | 109/- H |
| **L-Diformylcystine** | 91/- D |
| **2, 4-Dimethoxy-benzaldehyde** | 120/- H |
| **2, 4-Dimethyl thiazole** | 35/- D |
| **L-Diphenacetylcystine** | 59/- D |
| **Diphenyl phosphoryl chloride** | 42/- H |
| **Ethyl *iso*butyl ketone** | 170/- H |
| **2-Ethyl hexoic acid** | 32/- K |
| **Flavin adenine dinucleotide** (FAD)(85% ± 5%)(25 mgm. amps.) | 138/- A |
| **Hexamethylene dibromide** | 40/- H |
| **Hexamethylene dinitrile** | 93/- H |
| **Hydrobenzoin** | 35/- D |
| **p-Hydroxy-phenylacetic acid** | 39/- D |
| **L-Leucine (free from methionine)** | 62/- H |
| **Methyl formanilide** | 150/- K |
| **O-Methyl-DL-serine** | 8/- G |
| **N-Morpholylacetal** | 185/- H |
| **m-Nitrobenzonitrile** | 36/- D |
| **4-Nitropyridine-N-oxide** | 19/- D |
| **5-Nitro-quinoline** | 38/- D |
| **Potassium phenolphthalein di-sulphate** | 50/- D |
| **Pyridine-2-aldoxime methiodide** (2-PAM) | 197/- G |
| **Pyridine-2-aldoxime** | 65/- H |
| **Pyridine-3-aldoxime** | 80/- H |
| **Pyridine-4-aldoxime** | 75/- H |
| **Pyridine-2, 6-dialdoxime** | 110/- H |
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# LABORATORY BDH CHEMICALS

**N-Methyl-N-nitroso-toluene-p-sulphonamide**

$CH_3.C_6H_4.SO_2.N(CH_3).NO$

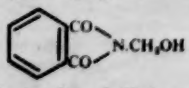
Diazomethane, well known as a valuable and versatile reagent, can be generated easily and safely in solution in ether or in ether and alcohol by treating *N*-methyl-*N*-nitroso-toluene-*p*-sulphonamide with potassium hydroxide in a suitable medium (de Boer and Backer, *Proc. Koninkl. Ned. Akad. Wetenschap.*, 1952, **55B**, 444; *Rec. trav. chim.*, 1954, **73**, 229).

The sulphonamide is issued in very pale yellow crystals, melting point 58-60° C.

10 g 6/6 25 g 13/- 100 g 44/6

*Packages extra, returnable*

**N-Hydroxy-methyl-phthalimide**



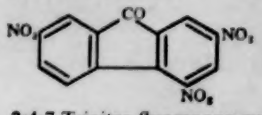

Winstead and Heine (*J. Amer. Chem. Soc.*, 1955, **77**, 1913) have shown that *N*-hydroxy-methyl-phthalimide is a valuable reagent for the identification of amines. The amine to be identified is refluxed with a 10% solution of hydroxymethyl-phthalimide in 80% ethanol for ½-2 hours and the *N*-arylamino-methyl-phthalimide separates as a crystalline product on cooling. The thirty derivatives prepared by Winstead and Heine melt in the range 112° C to 242° C.

*N*-Hydroxy-methyl-phthalimide is supplied as an off-white, crystalline powder, melting point 142-144° C.

5 g 3/9 10 g 6/9 25 g 13/3

*Packages included*

**2:4:7-Trinitro-fluorenone**




2:4:7-Trinitro-fluorenone, supplied as a pale yellow crystalline powder, melting point 175-6° C, forms stable complexes with a wide variety of aromatic hydrocarbons and derivatives. The complexes are readily prepared and generally melt sharply without decomposition. Apart from their use for identification, they can be employed in purifying certain aromatic hydrocarbons, since the hydrocarbon portion of the complex can be recovered by passing a solution of the complex over activated alumina. Alternatively, the complex may be reduced, giving an acid-soluble product from the trinitro-fluorenone moiety.

There are references in the literature to over a hundred substances known to form complexes with 2:4:7-trinitro-fluorenone. A bibliography will be supplied on application.

1 g 4/9 5 g 17/3 10 g 33/-

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